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APPLIED EPIDEMIOLOGY IN A GENERAL HOSPITAL

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Epidemiology has been defined by Hirsch¹ as "a science which will give, firstly, a picture of the occurrence, the distribution and the types of the diseases of mankind in distinct epochs of time and at various points of the earth's surface; and, secondly, will render an account of the relations of these diseases to the external conditions surrounding the individual and determining his manner of life."

As applied to a small community, such as a general hospital, it is with this second phase that epidemiology is concerned chiefly. Among its primary objectives become the exposing of the transmission paths of disease, or the recognition of conditions which may affect adversely the health of this particular community. Although such studies ordinarily are prompted only by the occurrence of actual cases of illness, there is no necessary reason why this should be so. If the epidemiologic approach is to have preventive application, potential hazards must be considered to be equal in importance to those which may have resulted in demonstrable actual damage. The mere fact that a fire has not occurred does not lessen the importance of searching for and eliminating fire hazards. The fact that no one has yet been killed does not warrant neglecting the hazards of accident. Unless we adopt the preventive point of view in epidemiology we will go along with smug satisfaction, thinking that all is well because no epidemic has occurred. Yet sporadic cases demonstrate as effectively as do epidemics that paths of transmission are open. By careful study of these cases we should be able to detect and to control the transmission paths, thus effectively preventing or limiting epidemic outbreaks.

ANCIENT METHODS

The epidemiologic possibilities become evident if we strip the veneer from the modern hospital and consider some of its basic features. Herodotus, speaking of ancient Babylon, said that the sick were carried to certain streets, where those who passed by inquired concerning their ailments. If any one had suffered a similar affliction, he told the sufferer what remedy or mode of treatment had proved beneficial in his own case. It was illegal for a visitor to refuse to listen to the recital of complaints as made by the patients. At

various temples of antiquity a somewhat similar procedure developed, except that the patients inquired of the deity to whom the temple was dedicated, or they slept in the presence of the sacred image. Later, special porticoes or pavilions within the temple area were provided where the sick were permitted to place their beds and where they were cared for by members of their own family. Eventually there appeared a group of individuals who specialized in knowledge concerning the relief of suffering and who were the forerunners of our medical profession of today.

In these ancient centers where the sick were concentrated the following features may be noted: (1) the patients, (2) the families of the patients acting as practical nurses, (3) the throngs of passers by, (4) the vehicular and animal traffic, e.g. ox-carts, beasts of burden, dogs and other small animals which passed to and fro along with the human traffic, (5) the food vendors, who carried viands kept warm by means of small charcoal burners, (6) the water carriers, usually slaves, who in jars or skins brought water for drinking or other purposes, and (7) the scavengers, usually slaves, who removed receptacles of excreta and other filth.

These various features are mentioned because, stated thus, one can see at once how much the patient was in contact with the entire community, the epidemiologic possibilities of such contact being quite obvious.

THE MODERN HOSPITAL

Yet these various features have their counterpart today. The modern hospital is but a hotel where sick folk may live and where facilities are provided for convenience in administering personal care and treatment. The street of antiquity has given place to the corridor along which today, as in ancient times, passes a constant stream of traffic, e.g. nurses, maids, orderlies, patients, physicians and interns, visitors. In one 900 bed state hospital studied, approximately 900 individuals are directly involved in its operation. The average daily census of patients is 742. The outpatients return to the various services at an average rate of 100 daily. The visitors average 400 daily. This hospital, in reality, is a small village with a population on any given day of well over 2,000 persons. Thirty-minute counts of pedestrian traffic were made over an interval of ten days, the counts being made at staggered periods which excluded the mealtime rush. In the main corridor along which the bulk of the traffic moves, individuals passed the observation point, during the time periods recorded, at a rate of more than 400 an hour.²

The traffic in the corridors of the patient floors is considerably less, but when one adds the activities of the 400 visitors to those of the personnel engaged in

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1. Hirsch, August: Handbook of Geographical and Historical Pathology, London, New Sydenham Society, 1883.

2. Rooks, Ronald: Air-Borne Transmission of Disease, to be published.

the routine service of the hospital the traffic at any floor level is surprisingly heavy.

The vehicular traffic in hospital corridors is by no means negligible, e. g. patient carts, wheel chairs, laundry, diet and scrub carts. For the food vender of antiquity, we substitute the diet kitchen staff with its distribution carts. Water carriers and scavengers in the modern hospital have been supplanted only in part by plumbing systems. The direct handling of objectionable matter cannot be eliminated entirely. It is a curious fact also that the modern hospital preserves a physical similarity to the ancient one in its pattern. The individual rooms designed for the sickest patients open directly on the corridor, i. e. the street. The wards are but blind streets, separated from the thoroughfare by short hallways, oftentimes with service rooms on either side.

HEALTH HAZARDS

If this comparison with the ancient hospital is kept in mind, it is easy to visualize epidemiologic possibilities which otherwise tend to be obscured by the elaborateness of the modern institution. We must consider the general hospital to be a concentration point for individuals of lowered resistance. In either their present or past illnesses these patients often contribute to the hazards of their new environment. On the other hand they may be subjected at this concentration point to increased health hazards, which include a fair sampling of the transmissible diseases current in the community in which the hospital is situated. It must be remembered that all of the personnel engaged in the operating of a hospital have their homes in that community and participate in the various community activities. As a consequence, the separation between the hospital patients and the community is more imaginary than real. This is true of all hospitals, the difference lying chiefly in volume. The basic problems are common to all.

Entrance into a hospital is occasioned by the illness of the patient and, ordinarily, some element of urgency is involved. Under these conditions, except for cases of recognized communicable disease, epidemiology is usually most remote from the present interest of either the patient or the attending medical or surgical staff. The patient desires relief, not epidemiology. Thus, quite unawares and unintentionally the patient may introduce infections which interfere with the functions of the hospital even though they may not happen to result in important damage. The epidemic of scarlet fever and of hemolytic streptococcus infections in a maternity ward recently described by Diddle, Trussell and Plass³ was brought about by an expectant mother who was admitted to the maternity ward with an infection of the upper respiratory tract following exposure to scarlet fever in her own community. No one had any knowledge of this exposure until several weeks later, when the epidemiologic studies brought this point to light.

A child was brought to the orthopedic service, having been previously exposed at home to chickenpox. In the absence of knowledge of such exposure, he was placed in a small ward with the result that several cases of this disease developed among children in that group. In a distant ward two additional cases developed in children who possibly may have received their infection from him, although the channel through which such infection passed was not definitely proved. The development of eruptive disease in children encased in plaster casts complicates the problem of their care.

Repeatedly, children have been received who at the time were in the incubatory stage of measles. Prior knowledge of exposure to this disease does not always exist, but accurate histories relative to previous attacks enable one quickly to locate the susceptible, should a case of the disease develop. With such knowledge, immediate and effective measures are possible to prevent or to reduce the severity of the disease in the susceptible group.

On various occasions, individuals ill with other diseases have been admitted in ignorance of the fact that they were typhoid carriers. One need not dwell on the risk involved in handling such cases in the general wards, at least without adequate precautionary attention on the part of those immediately involved in their care. It would seem logical that all persons who have ever had typhoid and all patients with gallbladder disease should be studied to ascertain whether they are typhoid carriers.

It is common knowledge that in a general hospital which does not accept known cases of pulmonary tuberculosis the nurses and interns develop infections, as is indicated by the change in their reactions to the Mantoux test. As this change is not shared to a comparable degree by the students of the same age group in the same community, there is reason to suspect that patients with whom they are in contact may be spreaders of the disease. Obviously, patients with open tuberculosis who gain admittance to a general hospital bring their infection with them and add to the hazards of their new environment.

The hazards to patients in the new environment may be connected with the physical or routine aspects of the hospital. Recently, during the routine testing of the circulating ice water in a general hospital, evidence of contamination was found. Investigation disclosed that one of the services requiring cool water for washing some films had attached a rubber tube to the ice-water tap and led the water to the bottom of a small vat. With an open faucet valve, this constituted a perfect setup for back siphonage when and if a negative pressure developed in the water line. Evidently some back siphonage had taken place. Although in this particular instance no known damage resulted, numerous possibilities for back siphonage exist in most hospitals unless very painstaking search has been made to ensure their elimination. In one hospital it was necessary to install more than 600 vacuum breakers to eliminate potential back siphonage.⁴ Even so, the human element is difficult to control. In the laboratories, individuals who are unfamiliar with the possibilities of back siphonage are very likely to set up apparatus which creates the conditions for such development. In other instances, individuals may interfere with corrective devices. For example, an air breaker was installed on a bed pan washer to make back siphonage impossible. A student nurse who disliked the noise restored the original hazard by the liberal application of adhesive tape to the air breaker.

However, most of the hazards are connected with individuals rather than with mechanical devices. Godfrey and Pond⁵ recently reported a small epidemic of Flexner dysentery caused by contamination of the ice supply in a hospital. The situation which they described exists in most hospitals, and the hazards are increased

3. Diddle, A. W.; Trussell, Ray E., and Plass, E. D.: Scarlet Fever in Obstetrics, *Am. J. Obst. & Gynec.* 39: 608-617 (April) 1940.

4. Baxter, A. C.: Personal communication to the author.
5. Godfrey, E. J., and Pond, M. A.: A Hospital Epidemic of Flexner Dysentery Caused by Contaminated Ice, *J. A. M. A.* 114: 1151-1154 (March 30) 1940.

whenever ambulant patients are given access to the service rooms, as not infrequently is the case when they are rendering assistance to other patients.

Perhaps the center of greatest potential danger to any hospital is its otolaryngology service. Many of the operative cases there represent sequelae to some infectious disease. Hemolytic streptococci abound in the draining lesions of such patients. Many patients are children who, because of the difficulty of controlling them, may spread their infections to others. Scarlet fever, streptococcal sore throats and erysipelas are among the infections which result. In one instance investigated a series of five patients with scarlet fever and one with hemolytic streptococcus sore throat were shown to have had close contact with a patient suffering from discharging ears. When a culture was found positive and the patient was removed to isolation, further infections ceased.

That visitors may introduce infections to the patients whom they visit is an obvious possibility. The wonder is that such infections are not more numerous than they are. It is through the visitors and the employees that the patients share directly in the current health problems of the community. Recently a child in the orthopedic ward was visited by his father, who, as was ascertained later, was suffering from mumps at the time of his visit. In due time the child developed mumps, as did four other children with whom he was playing in the ward.

RESPONSIBILITY OF THE HOSPITAL

The general hospital, being a concentration point for the community illnesses, has also an opportunity and a responsibility to serve the community along the lines of epidemiology. A patient from another city entered the hospital suffering from amebic dysentery. In connection with his history, special attention was paid to epidemiologic aspects. It was found that he worked as a cook at one restaurant and his wife was employed at another. It became the duty of the hospital to acquaint the local health authorities with the situation in order that appropriate decisions might be made.

A woman who entered with chronic bacillary dysentery gave a history of working as a pastry cook in the dining service of a small college. In releasing such a patient to return to the same danger point, the hospital would assume a responsibility which it has no right to assume. The local health authorities should decide the conditions under which she may resume her occupation.

A woman entered the hospital for a small operation, received appropriate and successful treatment, and was discharged. On her history sheet, among the past diseases, appeared a record of typhoid suffered many years previously. Scant attention appears to have been paid to this item and, if any laboratory studies were made, it is not a matter of record. This is unfortunate, because within a few years she was proved to be the source from which an epidemic of typhoid developed. At that time there was reason to believe that she had been a carrier for many years. An epidemiologic study of the patient at the time of hospitalization might have resulted in averting the calamity.

Recently a group of five students from various parts of a university community entered the isolation hospital suffering from scarlet fever. A sixth student, daughter of a physician, was taken home by him because of the same disease. Through epidemiologic investigation of these cases it was learned that the one common activity was the eating of meals at a certain restaurant

within the incubation period of their disease. In gathering this information, a clue was secured as to two possible concealed cases among the employees. The local health officer, on being acquainted with the situation, confirmed the presence of the two affected employees and forced their isolation.

An epidemiologic service in a general hospital affords an opportunity for gaining experimental knowledge as to the mode of spread and practical methods of control of the various diseases studied. Propinquity does not necessarily mean effective exposure. Aerial transmission even within the same room is not so frequent as one might suppose. The studies of Rooks² and of MacDonald⁶ suggest that one might remain in a scarlet fever ward for as long as six hours before inhaling a single hemolytic streptococcus. Except when viruses are concerned, the direct implantation of the causative organisms appear usually to be a prerequisite for the spread of upper respiratory infections. By basing measures on this hypothesis it is possible oftentimes to effect a satisfactory degree of control without closing wards except for the time required for the investigation.

These brief illustrations typify what one may expect to find in any general hospital if epidemiologic study is made of the patients, personnel and hospital environment.

Responsibility for such studies should be centered in some one individual, who should have access to all services of the hospital, who will coordinate such investigations as may be necessary, and who will receive the fullest support from the heads of the departments concerned. It is feasible to report to him all cases of evident epidemiologic importance and to seek from him advice as to cases of dubious status. Responsibility should be placed on him to investigate the potential health hazards existing in the institution. When actual cases of communicable disease develop in the hospital, the affected wards should be closed as a matter of routine until his investigations have been made. His should be the responsibility of deciding on the measures needed to ensure that the hospital's functions may proceed safely and with the least possible delay. One of his duties should be to train the interns to recognize the epidemiologic possibilities in the situations faced and in the patients handled.

Centralization of responsibility is advisable because epidemiologic trails cross artificial boundaries in the hospital just as they do in larger communities. The individual case may develop in one ward but the trails may lead anywhere throughout the hospital or even into the surrounding community. Moreover, hospital epidemiology is quite complicated. The constant flow of visitors, the shifting of hospital personnel from ward to ward, the ingress and egress of patients tend to obscure the trails which a disease may have followed. However, in the absence of some great calamity we shall remain ignorant of the potential health hazards in these institutions until we make a serious attempt to uncover these trails. In particular instances we may fail to solve the epidemiologic problems. In fact, we may expect such failures to outnumber the successes. Nevertheless, in the effort to solve these problems we are certain to find potential transmission paths which need to be guarded, and we can work out procedures adapted to the existing situations which will reduce to the minimum the health hazards suggested in this discussion.

6. MacDonald, Kenneth: Air-Borne Beta Hemolytic Streptococci: A Scarlet Fever Epidemic, *Am. J. Hyg. (Sec. B)* 31:88 (March) 1940.

SUMMARY

As applied to a small community, a primary objective of epidemiology is the exposing of the transmission paths of disease or of conditions effecting adverse mass action in that community. Although such studies ordinarily are prompted by the occurrence of actual cases, there is no necessary reason why this should be so. If the epidemiologic approach is to have preventive application, potential hazards must be considered of epidemiologic importance whether or not resulting in demonstrable actual damage. The general hospital is a concentration point for individuals of lowered resistance. In either their present or past illnesses, these patients oftentimes contribute to the hazards of their new environment. On the other hand, in their lowered state of resistance they may be subjected at this concentration point (hospital) to increased health hazards representing a fair sampling of the diseases prevalent in the entire community.

Health hazards originate in patients, visitors, the hospital personnel or in the physical setup of a hospital. Because of their sporadic occurrence, attention usually is not directed to the avenues whereby infections are transferred. Thus these transmission paths remain undetected even though open. In a general hospital of moderate size the problems encountered justify placing the responsibility for current epidemiologic service on some definite staff member for the better protection of the patients, of the hospital personnel and of the community.

ABSTRACT OF DISCUSSION

DR. W. G. SMILLIE, New York: Dr. Barnes's conception of a modern hospital corridor as the arcade of a busy city is appropriate. The analogy applies also to certain other institutions, such as universities and large factories. These cohesive, closely knit units of our social fabric offer excellent opportunities for epidemiologic study. Dr. W. H. Welch defined epidemiology as "the study of the natural history of disease"; thus there is an epidemiology of cancer and of heart disease, as well as of dysentery and tuberculosis. There is an epidemiology of industrial accidents as well as an epidemiology of syphilis. Whenever groups of people are living and working in small, integrated social units, subjected to uniform environment, their activities and their contacts so controlled that they may be subjected to exact appraisal and analysis, conditions are ideal for epidemiologic study. It is generally believed that a successful epidemiologic study requires a massive accumulation of data, which will be appropriately analyzed and interpreted. The fallacy of this conception was emphasized years ago by Ezra Hunt, at the first meeting of the American Public Health Association in 1872, who said: "A great number of cases to observe is in some respects valuable, but confusion and difficulty of study sometimes arise from too great aggregation of disease under the extra artificial conditions of cities (contagious disease) hospitals, and so forth, and very much is to be learned from a few typical cases occurring under circumstances less complicated. There is often not so much to be learned by observing a very great number of cases as by an exhaustive searching into a few cases, all the facts of which are more within the grasp." In his paper, Dr. Barnes has applied the criteria of Ezra Hunt.

Rural Health Administration.—The establishment of local boards of health represents the first official attempt to attack rural health problems in America. These boards have been in existence for more than one hundred years and in some rural areas they still function in very much the same manner as they have through the generations. The first local boards of health were established in Massachusetts in 1797. Connecticut followed in 1805.—Smillie, Wilson G.: *Public Health Administration in the United States*, New York, Macmillan Company, 1940.

PERFORATING GUN SHOT WOUNDS
OF THE ABDOMEN

AN ANALYTIC STUDY AND STATISTICAL REVIEW
OF TWO HUNDRED AND NINETY-TWO CASES

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Injuries and deaths resulting from gun shot wounds should be of vital interest to every one, since at the present time over half of the world is engaged in war and the peace of the rest of the world hangs by a thread. Perforating gun shot wounds of the abdomen should be of special interest to the general surgeon because the mortality rate has not been greatly lowered during the past twenty-five years and, therefore, this type of injury remains the most effective method of killing. Although surgical judgment and technic have improved, there has also been a corresponding increase of 20 per cent in the velocity of the bullet, which causes more damage to the abdominal organs. Fortunately, the incidence in civil practice is rare.

MATERIAL REVIEWED

This paper is based on a study of 292 cases of gun shot wounds of the abdomen with visceral perforations which occurred in Nashville, Tenn., during the period of 1923-1939. Of the twenty-four cases in which exploration was not done there were twenty-three deaths, or a mortality of 95.8 per cent. However, of 268 cases in which exploration was done there were 166 deaths, or a mortality of 61.9 per cent. This is quite high, but not far out of line with the reports of other surgeons reporting on a large series from general hospitals. It should be emphasized that only those cases were considered in which there were visceral perforations, whereas in most reviews cases are included in which the abdominal wall and peritoneum had been penetrated without visceral perforation. By including the cases without perforation the mortality would obviously be lower.

After studying the peace time reviews of cases that occurred during approximately the same period as covered by this review, and including only cases in which a viscus was perforated, and further including only the series in which the total number of cases was over 100, it was discouraging to discover that the operative mortality remains approximately 60 per cent. This was found to be true of the report of Taylor¹ of Indianapolis, Loria² of New Orleans, Mason³ of Birmingham, Ala., and Oberhelman and LeCount⁴ of Chicago, as well as the combined statistics of men reporting cases from Charity Hospital of New Orleans. One of the few exceptions to this is the report of Billings and Walkling,⁵ reporting 114 cases from Philadelphia with an operative mortality of 48.2 per cent. This is the only large series reviewed showing an operative mortality below 50 per cent. There were

Read before the Section on Surgery, General and Abdominal, at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Taylor, Frederic W.: *Gun Shot Wounds of the Abdomen*, J. Indiana M. A. **31**: 342-345 (July) 1938.

2. Loria, F. L.: *Visceral Injuries in Gun Shot Wounds of the Abdomen*, New Orleans, M. & S. J. **80**: 283-289 (Nov.) 1927.

3. Mason, J. M.: *The Influence of Hemorrhage on the Mortality in Gun Shot and Other Injuries of the Abdomen*, Ann. Surg. **79**: 382-385 (March) 1924.

4. Oberhelman, H. A., and LeCount, E. R.: *Peace Time Bullet Wounds of the Abdomen*, Arch. Surg. **32**: 373-412 (March) 1936.

5. Billings, A. E., and Walkling, Adolph: *Penetrating Wounds of the Abdomen*, Ann. Surg. **34**: 1018-1043 (Dec.) 1931.

found several small series of selected cases in which the mortality was below 50 per cent, but these could not be called representative of the true state of affairs. For example, a review of the operative mortality at the Nashville General Hospital for one year gave only 35.7 per cent.

Since the mortality still remains high, we have tabulated and attempted to evaluate the results in this study, to the end that some conclusion may be reached as to the lack of progress in lowering the mortality.

The type of weapon used, the age, sex, color of the patients, and the viscera or vessels perforated are all factors influencing the mortality which are beyond the surgeon's control. However, the promptness of preparation for operation, choice of anesthetic, operative technic, length of procedure and preoperative and postoperative management are factors in the lowering of mortality that are under the surgeon's control.

INCIDENCE

The incidence of gun shot wounds of the abdomen is rare in most parts of the country as revealed by the statistics from the Metropolitan Life Insurance Company. However, in Nashville it ranks as one of the most frequent emergencies seen in the charity hospitals and occurs with six times the frequency of ruptured gastric ulcer and twice the frequency of ruptured duodenal ulcer. The number of cases has steadily increased in Nashville during the past fifteen years, and by grouping the cases in five year periods and comparing them, it was found that the incidence has increased 100 per cent, although during this period the population of the city has increased only 16 per cent (table 1).

It has been repeatedly said that the smaller the caliber of the rifle or pistol the lower the mortality, and this fact is borne out in the present review. Seventeen persons were shot with a 0.22 caliber rifle with a mortality of 41.1 per cent, 241 shot with pistols with a mortality of 63.4 per

TABLE 1.—Comparative Study of Incidence

Year	Total	Died	Lived	Mortality
1923-1924.....	14	10	4	71.4
1925-1929.....	60	36	24	60.0
1930-1934.....	97	64	33	65.9
1935-1939.....	121	79	42	65.2
Total—17 years.....	292	189	103	64.7

TABLE 2.—Type of Weapon, with Mortality

Weapon	Total	Died	Lived	Mortality
Pistol.....	241	153	88	63.4
Shot gun.....	34	29	5	85.2
Rifle.....	17	7	10	41.1

cent, and thirty-four injured by shot guns with a mortality of 85.2 per cent. The reason for the high mortality from shot guns was that most of these cases were attempted murder, shot at close range and tearing large holes in the viscus, making most of the wounds almost impossible to repair (table 2).

AGE, SEX, COLOR

The youngest person was 5 years of age and the oldest was 80 years of age, but the greatest number, 125, or 42.4 per cent, occurred between the ages of

21 and 30. It was interesting to note that the mortality increased steadily with the decades of life, the lowest rate, 50 per cent, occurred in the age group of 1-10 and the highest rate of 85.7 per cent between the ages of 61 and 70 (table 3). The lower mortality rate in the younger group could be accounted for by the fact that most of the accidental injuries from 0.22 rifles

TABLE 3.—Occurrence in Different Decades with Mortality

Decade	Total	Died	Lived	Mortality
1-10.....	6	3	3	50.0
11-20.....	30	29	21	58.0
21-30.....	125	76	49	60.8
31-40.....	61	42	19	68.8
41-50.....	29	23	6	79.3
51-60.....	11	9	2	81.8
61-70.....	7	6	1	85.7

TABLE 4.—Color and Sex with Mortality

Class	Total	Died	Lived	Mortality
Colored male.....	150	95	55	63.3
White male.....	93	64	29	68.8
Colored female.....	36	21	15	58.3
White female.....	13	9	4	69.2

were in this group. Also the increased stamina of youth probably enhanced the chances of recovery.

Similar to other reports, the greatest number of patients in our series were males, 243, or 83.2 per cent; forty-nine, or 16.8 per cent, were females. Ranked as to frequency there were 150 colored males, or 51.3 per cent, ninety-three white males, or 31.9 per cent, thirty-six colored females, or 12.4 per cent, and thirteen white females, or 4.4 per cent (table 4). It has been believed that owing to the well developed muscles of the average colored person as contrasted with white persons there is a lower mortality in the colored as the result of the fact that the bullet might be partly spent before it entered the abdominal cavity and was therefore not capable of doing as much damage. This assumption seems to have been supported in this review, as the mortality in the colored race was 62.3 per cent as contrasted with 68.8 per cent for the white race (table 5).

It was shown also that females tolerated abdominal injuries resulting from gun shot fire better than males, and the mortality in the female was 61.2 as against 65.4 per cent for the male.

ADVANTAGE OF EARLY OPERATION

The improvement in transportation has made it possible for the injured to arrive at the hospital within a short period of time, but it seems that there is still too much delay in the beginning of the laparotomy. This, in part, may be due to the fact that most of our cases came at night or on holidays when the efficiency of the personnel of the hospital was at the lowest ebb. Another factor that might have contributed to the delay was that the patient was usually first seen by an inexperienced intern who might not have fully appreciated the seriousness of the condition and might have underestimated the degree of shock.

Preliminary x-ray examinations may be of value in the determination of the possibility of questionable entrance into the abdominal cavity, but as a routine procedure this should be discouraged because of the imposed preoperative delay and the added moving and handling of patients, many of whom are in an extreme

degree of shock. The statistics in this review show that, the earlier the patient was operated on, the greater the chance of recovery. From an analysis of the records of 112 patients who were first seen in the outpatient department of one of the hospitals, it was found that of those in a serious condition and dying within six

TABLE 5.—Comparative Study of Color and Sex

Classification	Total	Died	Lived	Mortality
Colored male and female.....	186	116	70	62.3
White male and female.....	106	73	33	68.8
Colored male and white male.....	243	159	84	65.4
Colored female and white female..	49	30	19	61.2

TABLE 6.—Length of Time Before Operation, with Mortality

Hours	Number	Died	Lived	Mortality
0-2.....	115	69	46	60.0
2-4.....	83	52	31	62.6
4-6.....	20	13	7	65.0
6-9.....	14	10	4	71.4
Over 9.....	10	6	4	60.0

hours of admittance to the hospital 30.7 per cent had been given x-ray examinations. I believe that this loss of time necessary for preliminary x-ray examination contributed more to the mortality of these patients than was justified by the diagnostic aid to the surgeon at the time of exploration, for the experienced surgeon regularly examines all of the intestinal tract.

Accurate data were kept on the length of time elapsing from the receipt of injury to the beginning of the operation and showed convincingly the advantage of early operation; for in those operated on within two hours the mortality was 60 per cent and the fatality rate increased steadily as time elapsed until with an interval of from six to nine hours the mortality was 71.4 per cent (table 6). After nine hours the mortality again was lowered to 60 per cent. Apparently this was due to the fact that large hemorrhage had not occurred in many of these cases.

AMOUNT OF HEMORRHAGE

It has been shown by Mason, by Loria⁶ and by this study that the amount of hemorrhage is the greatest single factor in the determination of the mortality. Therefore, when a patient is seen in shock following gun shot injury of the abdomen it is safest to assume that this shock is due to actual blood loss and prepare the patient for exploration as soon as the blood pressure has been raised to a level at which a laparotomy can be fairly safely performed. However, this opinion is not shared by all and there have arisen two schools of thought in the management of such patients, the first, as already advocated, treating the patient for shock in the operating room and performing exploration at the earliest possible moment to check active hemorrhage, the second assuming that the shock is primary and deferring operation for several hours while combating shock.

The presence of blood in the abdominal cavity was recorded in 222 cases in the series under analysis. The amount of blood was estimated by the surgeon as large, moderate or small. We have used the same classification as other men have used; namely, large

hemorrhage group 1,000 cc. or more, moderate hemorrhage from 500 to 1,000 cc., small hemorrhage 500 cc. or less.

There were 112 cases in the large hemorrhage group, with a mortality of 83.9 per cent (table 7).

In the moderate hemorrhage group there were forty-eight cases with a mortality of 60.4 per cent and sixty-two cases in the small hemorrhage group with a mortality of 43.5 per cent. This study shows convincingly that the amount of hemorrhage is the greatest individual factor in the mortality irrespective of the organ damaged.

VALUE OF TRANSFUSION

It was a difficult task to find suitable donors in a short period of time, as there were no available funds for the use of professional donors at the Charity Hospitals, where the greatest number of these cases occurred. However, ninety-nine (30.4 per cent) of the 292 patients were given transfusions for from one to ten times, which affords a sufficient number of cases to study the value of this procedure.

In the large hemorrhage group forty-seven, or 41.9 per cent, of the total group were given transfusions with thirty-five deaths, or a mortality of 74.4 per cent. In contrast to this there were the sixty-five cases in which transfusions were not given, with a mortality of 90.7 per cent (table 8). In this group the mortality was lowered 16.3 per cent by transfusion.

In the moderate hemorrhage group thirty patients were given transfusions, or 62.5 per cent of the total, with nineteen deaths, or a mortality of 63.3 per cent; but eighteen patients were not given transfusions, with ten deaths, or a mortality of 55.5 per cent. In this group there was no lowering of the mortality.

In the small hemorrhage group twenty-two, or 35.4 per cent, were given transfusions, with eight deaths, or a mortality of 36.3 per cent, as against forty not given transfusions, with nineteen deaths, or 47.5 per cent. In this group the mortality was lowered 11.2 per cent.

TABLE 7.—Amount of Hemorrhage, with Mortality

Amount	Total	Died	Lived	Mortality
Large.....	112	94	18	83.9
Moderate.....	48	29	19	60.4
Small.....	62	27	35	43.5

TABLE 8.—Study of the Value of Transfusion

Group	Transfused			Not Transfused		
	Number	Died	Mortality	Number	Died	Mortality
Large.....	47	35	74.4	65	59	90.7
Moderate.....	30	19	63.3	18	10	55.5
Small.....	22	8	36.3	40	19	47.5
Total.....	99	62	63.5	123	88	71.5

In the total it was found that of the ninety-nine given transfusions the mortality was 63.5 per cent; in the 123 not given transfusions the mortality was 71.5 per cent. Thus in those who received blood the mortality was 8 per cent lower than in those not receiving blood.

ORGANS PERFORATED

Next to hemorrhage the most important factor in the death rate is the organ or organs perforated. The mortality increases when more than one organ is per-

6. Loria, F. L.: The Influence of Hemorrhage in Abdominal Gun Shot Injuries, *Ann. Surg.* 96: 169-178 (Aug.) 1932.

forated, as the number of holes and degree of destruction of the organs increase and as the site of perforation descends in the intestinal tract. The lowest mortality was in perforation of the liver, 44.4 per cent, and then the mortality steadily increased as the stomach, small intestine and large intestine were reached. The mortality of perforation of the large intestine was 65.9 per cent (table 9).

The small intestine was perforated most often, 136 cases with an average number of holes of 6.2, the large intestine next with eighty-nine cases giving an average number of holes of 2.5, and last the stomach with sixty-eight cases giving an average number of holes of 2.05.

OPERATIVE PROCEDURE

Simple closure is the best procedure for perforation whenever possible, for any attempt at resection is associated with high mortality. However, this becomes necessary at times when the blood supply to the intestine is destroyed or a considerable portion of the intestine is shot away. There were thirty-three cases in which a portion of the intestine was resected varying from several inches to several feet with twenty-seven deaths, or a mortality of 81.8 per cent. In case of

TABLE 9.—Mortality of Perforation of Different Organs

Organ	Single Organ			Two or More Organs		
	Total	Died	Mortality	Total	Died	Mortality
Liver.....	18	8	44.4	33	22	66.6
Stomach.....	15	8	53.3	46	30	65.2
Small intestine..	61	39	63.9	72	50	69.4
Large intestine..	29	19	65.5	57	38	66.6
Spleen.....	6	3	50.0	5	5	100.0
Kidney.....	6	3	50.0	13	6	46.1
Bladder.....	2	12	9	75.0
Pancreas.....	3	1	33.0
Large vessels...	4	4	100.0

severe damage to the movable portion of the large intestine it is advisable to bring the damaged portion outside the abdominal cavity rather than to try and do a resection. Six splenectomies with five deaths, or a mortality of 83⅓ per cent, were performed. There were also thirty-three cases with associated chest and abdominal injuries giving twenty-eight, or 81.7 per cent, mortality.

ANESTHETIC

Ether was the anesthetic of choice, as it gave the required relaxation not associated with very much shock. Spinal anesthesia was only occasionally used, as it causes too much drop in the blood pressure, which is often already at a dangerously low level. Another practical objection to spinal anesthesia is the fact that it may cause contraction of the intestine, forcing more of the intestinal contents out into the abdominal cavity. Local and gas anesthesia did not give the proper relaxation and made it necessary for the operator to fight the intestine, causing further shock and squeezing more material out into the peritoneal cavity. Ether was used in 244 cases, with a mortality of 61 per cent; in the remaining twenty-four cases in which local, gas or spinal anesthesia was used the clinical notes were insufficient for accurate statistical analysis.

Paradoxical as it may seem, the mortality decreased in inverse proportion to the length of the operation (table 10).

In the short operations of less than thirty minutes the mortality was 77.7 per cent, and the mortality

was gradually reduced as the length of the anesthetic increased until the lowest rate was between ninety-one and 120 minutes, when the mortality was 54 per cent. After two hours the mortality again increased and this probably can be explained by the fact that the operator was exceedingly slow or there was a great deal of

TABLE 10.—Length of Operation, with Mortality

Time	Number	Died	Lived	Mortality
0 - 30 minutes.....	9	7	2	77.7
31 - 60 minutes.....	84	53	31	63.0
61 - 90 minutes.....	80	48	32	60.0
91 - 120 minutes.....	50	27	23	54.0
121 - 180 minutes.....	21	14	7	66.6

damage to repair. The high mortality in the operative group requiring less than one hour can be explained by the fact that, first, in the most serious cases death occurred within thirty or forty minutes; in nineteen of the operative cases, death occurred on the operating table. Secondly, the hasty operator is more likely to overlook perforations, and it is not of much value racing against time to close eight or ten perforations and leave one not closed. In the twelve autopsies performed in cases in which the operations had been completed, overlooked perforations were found in six, or 50 per cent, and four of these six, or 66⅔ per cent, were found in operations requiring less than one hour. It should be emphasized that slowness is not a virtue, but in an attempt to secure speed the operator should not sacrifice thoroughness.

CAUSE OF DEATH

In the 189 cases in which death occurred, the time elapsed between the operation and death varied from a few minutes on the table to ninety-three days. The vast majority of patients died within twenty-four hours. It cannot be determined accurately whether a patient dies of shock and hemorrhage and when peritonitis supervenes, and there is undoubtedly an overlapping and combination of all these factors. I have arbitrarily classed those dying within twenty-four hours as dying of shock and hemorrhage, and those after twenty-four hours as dying of peritonitis or some other cause than shock (table 11).

Table 11 shows that in 59.8 per cent of the fatal cases the cause of death was shock and hemorrhage

TABLE 11.—Cause of Death

Cause	Total	Mortality
Shock and hemorrhage.....	113	59.8
Peritonitis.....	56	29.6
Pneumonia.....	5	2.7
Gas bacillus.....	5	2.7
Other causes.....	4	2.2
Exhaustion.....	3	1.5
Intestinal obstruction.....	3	1.5

and in 29.6 per cent peritonitis. Only a small percentage of deaths were due to other causes. It is interesting to note that there were no records of any deaths from tetanus and only five from gas bacillus infection. In the last three years there have been no deaths due to gas bacillus infection. Shortly after sulfanilamide was given to the medical profession in this country it became my routine practice to use this agent in large doses intraperitoneally at the time of operation. This was supplemented by parenteral use of sulfanilamide

postoperatively. The prompt use of this drug was, I believe, undoubtedly of considerable value in combating infection.

Of the 103 patients who lived, the period of hospitalization varied from eight to 105 days, the average length of time being 29.1 days.

SUMMARY

1. Two hundred and ninety-two cases of gun shot wounds of the abdomen with visceral perforations were studied.
2. The smaller the caliber of the pistol or rifle, the lower was the mortality.
3. The mortality increased steadily with the decades of life.
4. The greatest number of patients were males, 83.2 per cent; 60.2 were Negroes.
5. The statistics in this review showed that, the earlier the patient was operated on, the greater was the chance for recovery.
6. The amount of hemorrhage is the greatest single factor in the mortality irrespective of organs damaged.
7. Ninety-nine patients were given transfusions and in this group apparently the mortality was lowered 8 per cent.
8. The mortality increases when more than one organ is perforated, as the number of holes and degree of destruction of the organ increase, and as the site of the perforation descends in the intestinal tract.
9. Paradoxical as it may seem, the mortality decreased in inverse proportion to the length of the operation.
10. Shock and hemorrhage accounted for the greatest number of deaths.

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ABSTRACT OF DISCUSSION

DR. ADOLPH A. WALKLING, Philadelphia: Whenever the abdominal wall has been penetrated by a bullet, exploration should be done. The patient may have signs of shock which may be due to fright, while the signs of perforation, such as pain, tenderness, rigidity and presence of air in the abdominal cavity, may be entirely lacking. When the patient is seen and his condition is satisfactory to withstand operation, no delay should be permitted. The most urgent problem is hemorrhage and it is difficult to differentiate hemorrhage and shock. At the Pennsylvania Hospital our mortality in the cases of severe hemorrhage was 61 per cent, in the moderate hemorrhage cases 39 per cent, and in the slight hemorrhage cases 26 per cent. The points made regarding multiple wounds and the fatal types of combined colon perforation with severe hemorrhage are well taken. That wounds in viscera may be overlooked and cause death was emphasized by Billings and myself in 1931. The more experience the operator has, the less are wounds overlooked. In the nine cases in which lesions were overlooked the condition was very critical at the time of operation and all were wounds of the upper abdomen. One can appreciate the difficulty of finding wounds of the kidney, pancreas and upper surface of the liver in a patient who has severe abdominal hemorrhage and whose condition is critical. Several of these had failed to show any reaction from shock after the use of the usual antishock measures, and their condition had rapidly changed from bad to worse because of continued bleeding, the operation having been done primarily for the control of hemorrhage. Under such circumstances the amount of the anesthetic and the time required for the operation assume more than the usual importance in the result. It is in such cases that blood transfusions will be of the greatest value. We have available in the blood bank at the Pennsylvania Hospital this morning 3,000 cc. of blood and 10,000 cc. of plasma. We prefer to give blood or plasma on the operating table. It is

our policy to explore the entire intestinal tract from the stomach to the rectum and to do it carefully and, if possible, inspect all organs and examine carefully for retroperitoneal hemorrhage. X-ray examination before operation in gunshot cases is a useless procedure. Our low mortality is due in a great measure to early operation and the liberal use of the blood bank for transfusions of plasma and blood.

DR. WALTER E. LEE, Philadelphia: The mortality from gunshot wounds of the abdomen in civil life has not been greatly reduced during the last twenty-five years. The unusual number of cases which Dr. Rippe reports does not make me envious, but I must confess surprise. His mortality of 61.9 per cent in gunshot wounds of the abdomen with visceral injury we match at the Graduate Hospital in Philadelphia with 53.2 per cent, slightly higher than Dr. Walkling's of 50 per cent, but it would seem that an average mortality of 50 per cent could be accepted in the United States at the present time. I agree with Dr. Rippe that the time interval between the receipt of the injury and the operation is the most important factor in influencing the end result. The better results which have apparently been obtained at the Pennsylvania and Graduate hospitals I feel are largely due to the emergency transportation service. Second in importance is the rapidity with which the operation is performed. The operating room is at all times prepared for such emergencies, and within thirty minutes after the request is made, night or day, the operating room will be ready to function. Next in importance is the availability and use of the blood bank for transfusions of whole blood and plasma, in the accident wards and the operating rooms. Last, but probably not least, in both of these hospitals for the last ten years residents in surgery, or fellows, have been in charge of the accident ward service, supplemented by staff assistants who make it possible at all times to operate within thirty minutes, if necessary. In my experience a patient who has not reached the operating room within two hours after the injury falls into the class of delayed operation. In our group there was only one patient who recovered when operated on four hours after the receipt of the wound. I agree with Dr. Rippe that, next to the time interval, hemorrhage is the most important factor in determining mortality.

DR. THOMAS M. JOYCE, Portland, Ore.: There are two important points which Dr. Rippe brought out, one of which has been brought out many times in the past, but no amount of repetition can overemphasize its relation to low mortality rates, and that is early blood transfusion. That the high mortality in gunshot wounds of the abdomen is directly proportionate to this factor has been understood for many years, but unfortunately, owing to the catastrophic suddenness of these cases and often to their economic status, it is impossible to procure blood when necessary. It is for this reason that the institution of blood banks in our larger hospitals and in many military medical units is to be highly praised. The other important point is the fact that mortality rates vary inversely to the length of time of the operation. I feel that this is merely another measure of the skill and care on the part of the surgeon. A hurried operation, a hurried, incomplete search and a hurried closure all leave opportunities for overlooking damage. The point is also brought out by Dr. Rippe's figures that there is a certain limit to which a patient can be subjected to a surgical procedure under anesthesia. It is after the second hour that the mortality again begins to rise. Dr. Rippe's paper brings out the importance of careful surgery, skillfully performed in the early stages, with proper attention to secondary factors of shock and hemorrhage.

DR. R. ARNOLD GRISWOLD, Louisville, Ky.: Penetrating wounds of the abdomen are one of the greatest problems in our large Southern city hospitals. Dr. Rippe's paper is an excellent summary of his experience in Nashville and there is nothing in it with which I disagree. When these patients come into the hospital they can be roughly divided into three groups: (1) the group with obvious penetration of the peritoneal cavity and perforation of or trauma to an intraperitoneal viscus, (2) the group with obviously no penetration and no intraperitoneal damage and (3) a group in which it is not at first evident whether or not there is visceral injury. In the

first group, most of the patients die of hemorrhage. That is not according to the experience of those who saw such patients in base hospitals during the war. Rapid, early operation is essential and, as Dr. Rippy says, the appearance of shock in these people is not primary shock, it is due to hemorrhage and there is no excuse for delaying operation in order to treat shock. Once the abdomen is opened, stopping the hemorrhage is the first consideration and closing the perforation is the second consideration. Perforation of large vessels must be dealt with rapidly. These are a few details of operation that I have seen neglected. One of the most frequent gun shot wounds is that of the kidney or kidney pedicle. This is best handled by reflecting the colon medially, just as one would free it for a resection, and doing anterior nephrectomy rather than turning the patient over. Another is a wound of the stomach on the posterior surface. One should not hesitate about splitting the anterior surface wide open instead of trying to get around to the back of the stomach. There is, however, a second group of cases in which there is penetration and perforation of a viscus that we do not operate on. Those are patients who have shot gun wounds with bird shot, and ice-pick wounds of the abdomen. Shot gun wounds at close range are such large wounds, tearing so many large vessels, with so much visceral damage, that repair of them is inadequate; it just doesn't work. In the patient who is shot by bird shot at far range, even though there is penetration of a hollow viscus, these wounds seal themselves much better than the surgeon can seal them by any operative measure. That also applies to wounds caused by the ice-pick, which is one of our most common Southern weapons. In cases which I feel do not immediately fall into one of these classes one has to wait to determine the exact status. Waiting too long in a penetrating wound of the abdomen is disastrous. Therefore within the last year in these borderline cases, which run from 10 to 20 per cent, I have used peritoneoscopy.

DR. LEO ELOESSER, San Francisco: Under optimal conditions in the best hospitals, with the best surgeons, the mortality of abdominal gun shot wounds is still appalling. The same holds true in military hospitals. I think that the reason is to be sought not in the promptitude with which the patients have come to operation but in the nature of the injury itself. Dumont of the Belgian Volunteers and Jolly of the Australian Volunteers in Spain, both with extensive experience in the treatment of abdominal war injuries, have stated that the fate of the abdominal injury is determined not so much by what is done as by the missile itself. In other words, if a man is wounded through the lower part of the abdomen, if besides a wound of the colon his large vessels are severed and he has a mesenteric tear with much hemorrhage, that man is going to die no matter whether one operates on him in a few minutes or in a few hours. If, on the other hand, a man is operated on who has, say, nothing but an injury to the liver, with some bleeding, he will probably live whether he is operated on early or late or whether he is not operated on at all. This has some bearing, I think, on the results of treatment not only in peacetime but much more so in wartime, because of the corollary that it is unwise to establish hospitals undertaking definitive treatment so close to the front as has been done in the past, with a view to treating abdominal injuries early. If the front line hospitals are established a little farther back we shall save many more patients by treating fractures efficiently than by attempting to treat abdominal injuries early. One other point: I think we may be a little too loath in these injuries to do enterostomies or colostomies or to extraperitonealize by packing off a conglomerate of intestinal coils badly damaged by a missile. If this was done more often, perhaps a few men might be saved who otherwise would be lost.

DR. ELKIN L. RIPPY, Nashville, Tenn.: In the Nashville General Hospital the mortality in the last three years has been lowered to around 51 per cent. This lowering of the mortality has been accomplished by the application of these principles: elimination of unnecessary handling, repeated transfusions, early exploration and the administration of sulfanilamide. Since preparedness is the keynote of America at the present time, let us as surgeons contribute our part by a thorough study of injuries as a result of gun shot fire.

HEAD INJURIES

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AND

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We are primarily concerned here with the management of patients with head injury admitted to the neurosurgical service at the Cook County Hospital. This service was formally established on Oct. 1, 1938. The present report is concerned with the patients admitted during 1939 (table 1).

In any statistical consideration of a series of patients the type of material and the criteria employed in the selection of cases are of importance. Our patients are admitted directly to the neurosurgical ward from the examining room of the hospital. They are persons who obviously have a head injury because of the external signs of trauma and patients who give a history of head injury followed by a period of unconsciousness.

A sizable group of patients have received a head injury but have no signs of cerebral damage. Another group are grossly intoxicated and, at the time they are seen in the examining room, it is impossible to tell whether or not they have a brain injury. These two groups are admitted for observation, and of course many of them later prove to have more or less serious cerebral

TABLE 1.—Results in 1,394 Cases of Head Injury Admitted to Cook County Hospital During 1939

Results	No. of Cases	Per Cent of Total
Recovered.....	1,111	79.7
Disabled.....	91	6.5
Dead.....	192	13.8
Within 6 hours after admission.....	45	3.3
Over 6 hours after admission.....	147	10.5

damage. Others do not and are dismissed after a brief period (from one to three days) of observation and x-ray examination of the skull.

In contrast to these we have a large group of elderly, ill nourished and debilitated patients in whom there is a high mortality from preexisting disease or from disease complicating their head injury. There were 479 patients (34.4 per cent of the total) in this series past the age of 50 (table 2). It will also be noted from table 2 that there were a large group of cases of unknown severely injured derelicts of whom we were unable to determine the age. There were 123 (8.8 per cent of the total) patients in this group with a mortality of more than 40 per cent. A large group of our patients are chronic alcoholic addicts. In this connection it is interesting to note that 545 patients (39.8 per cent) had the odor of alcohol on their breath at the time of admission.

These patients are all cared for in the services of the first two authors and are admitted in rotation to these services from the examining room of the hospital. We have pooled our statistics for the purpose of this report, and while there is no essential difference between the statistics for the two services it must be emphasized that

From the neurosurgical service of the Cook County Hospital and the Coroner's Laboratory of Cook County.

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the two services are conducted in the same ward and by the same nursing, intern and resident personnel but under the independent and individual supervision of the two authors mentioned. We have made no attempt to standardize our methods of treatment; we have made every attempt to make a statistical check against each other where there are differences in treatment.

Ideally, when a patient with a head injury first comes under observation an estimate should be made of the amount and extent of cerebral damage. Obviously, in many cases this cannot be done because of lack of adequate history, inability to carry out complete examination of the patient (because of shock and so on) and inability to correlate physical signs and symptoms with the organic brain injury present. From a practical standpoint some classification is essential and since 1934 we have used a purely clinical grouping. Our individual terminology has varied, but the grouping is the same: A, moribund patients, B, gravely injured persons, C, mildly injured persons and D, complicated cases. A fifth group of cases with late sequelae might be added, but obviously this is not of importance in the early management, except from the standpoint of prophylaxis. One of us (Verbrugghen) recently collaborated with

of a large "heat cradle," the source of heat being lighted electric bulbs. In cases of severe collapse, the patient is immediately placed in one of these without any attempts to remove his street clothing or to give him a bath. This is important, as well meaning nurses or attendants frequently add measurably to the patient's state of shock by unduly exposing him in their effort to remove his clothing, bathe him and otherwise "make him presentable." Obviously, if a patient is in shock the removal of his clothes and dirt, or even vermin, from his body should be postponed until his general condition has improved. One caution must be mentioned in connection with the use of external heat. Patients with brain injury, especially children, often have disturbance of the thermoregulatory mechanism. The rectal temperature should be taken hourly (every half hour in children), and as soon as it is over 100 F. the application of external heat should be discontinued. Other forms of heat, such as electric pads or hot water bottles, are equally efficacious. Some require greater caution to prevent burns of an unconscious patient.

Administration of fluid intravenously is often not only necessary but life saving to these patients. Obviously, large quantities of isotonic fluids should not be given to patients many of whom in a few hours will be liable to an increasing cerebral edema. Recent work (Coller and Maddock,² and White, Sweet and Hurwitt³) has shown the lack of necessity for administering sodium chloride unless there is abnormal loss of it, which is rare in these cases. Excessive chloride probably will promote development of edema in injured tissue. For this reason we prefer to administer dextrose dissolved in distilled water. A 10 per cent solution is mildly hypertonic and will at once increase fluid volume and reduce tissue edema. In our experience 1,000 cc. is an ample amount to give in most cases.

Stimulants are of value to the patient in marked collapse. Caffeine, nikethamide, strychnine or even powerful constrictors such as epinephrine or neosynephrin are used as indicated. Too rapid an elevation of blood pressure during the first few hours is to be guarded against, although doubtless its danger has been overemphasized.

Next to the immediate treatment of the shock or collapse, quiet is of the greatest importance in the management of a case of head injury. Manipulation of the patient is restricted to the minimum required for necessary examination and essential nursing care. X-ray examination is to be postponed until the patient is both out of danger and is conscious and cooperative. Attempts to obtain x-ray films earlier only endanger the life of the patient and usually end in failure because of lack of cooperation. The only exceptions to this rule are occasional special cases such as compound depressed fractures or suspected meningeal hemorrhage, and even here they are often better dispensed with. Until the patient has recovered from his initial collapse, surgical procedures including the suture of lacerations, reduction of other fractures or lumbar puncture must be postponed.

Sedatives are necessary in many cases and imperative in some. A wide choice is available. Morphine is always contraindicated at least in the early stages. We consider paraldehyde the most valuable single sedative

TABLE 2.—Distribution of Cases by Decades

Decades	Total Cases	Recovered	Died	Mortality Rate Per Cent
10-19.....	53	51	2	3.8
20-29.....	178	165	13	7.3
30-39.....	279	257	22	7.9
40-49.....	282	254	28	9.9
50-59.....	266	231	35	13.2
60-69.....	153	127	26	17.0
70-79.....	46	36	10	21.7
80-89.....	14	10	4	28.6
Unknown....	123	71	52	42.3
Total.....	1,394	1,202	192	13.8

the late Dr. Fantus in an outline of the therapy of head injury¹ that discusses the treatment appropriate to each of these groups.

In this article the treatment of head injuries is discussed from the following standpoints: (1) symptomatic, (2) control of intracranial pressure, (3) treatment of complications, both surgical and nonsurgical, and (4) the prophylaxis and treatment of late sequelae.

SYMPTOMATIC

First and foremost is the treatment of the collapse (shock) which is so prominent in the cases of group A (moribund) and of considerable importance in group B (grave injury). These patients should have the head lowered, especially those who are stuporous or comatose and are vomiting or have considerable mucus in the upper respiratory passages. They should be on their side or face to prevent aspiration of mucus or vomitus into the lungs. After vomiting has ceased and the patient has regained consciousness or at least regained his pharyngeal and laryngeal reflexes, he may be left flat in bed. Most conscious patients (adults) seem to prefer being flat with perhaps one pillow, and we believe that the preference of the patient may well be followed in this respect.

External heat is of great value in the early care of these patients. It is applied in our service in the form

1. Fantus, Bernard, and Verbrugghen, Adrien: The Therapy of the Cook County Hospital: Head Injuries, J. A. M. A. 114: 243-245 (Jan. 20) 1940.

2. Coller, F. A., and Maddock, W. G.: Water and Electrolyte Balance, Surg., Gynec. & Obst. 70: 340-354 (Feb., No. 2A) 1940.
3. White, J. C.; Sweet, W. H., and Hurwitt, E. S.: Water Balance in Neurosurgical Patients, Ann. Surg. 107: 438-457 (March) 1938.

in the great majority of cases. There is a wide margin of safety in its use and it is rapidly excreted, so that it will not mask developing stupor or coma longer than a few hours. For the latter reason it has to be repeated every few hours if the restlessness or delirium persists. It may be given by mouth or rectum and repeated as necessary.

Mechanical restraints are necessary as a precaution for all patients not constantly attended or perfectly conscious, rational and cooperative. They are not to be considered as a substitute for sedation, as the patient who is allowed to thresh restlessly in his restraints is harming himself by this activity as much as any other. In many cases they are a poor substitute for the constant presence of a nurse or attendant, and often they infuriate an otherwise tractable patient. They are a necessity when constant attendance is impossible for economic reasons; otherwise many embarrassing or serious accidents will occur.

The nursing care of patients with head injury, particularly those in coma, is of great importance. The care of the skin is as important here as with any other bedridden patient and may be made difficult by coma, incontinence and debility. The bladder and bowel also require special attention. The latter usually receives it because of the importance of catharsis or enemas in reduction of cerebral edema. The bladder may be neglected. Voris and Landes⁴ have shown by cystometric studies that most patients with acute brain injury have bladders which empty reflexly with from 150 to 200 cc. of filling. However, in contrast to this, others have an atonic bladder with no contractions with from 500 to 600 cc. of filling. One of us (Kearns) has pointed out that relatively slight obstruction of the urethra, such as mild prostatic hypertrophy or urethral stricture in the male or cystocele or rectocele in the female, may prevent reflex emptying of the bladder of comatose or stuporous patients. Palpation or percussion of the bladder alone is not sufficient to determine whether or not there is retention; the catheter must be used. Cystometry, if available, will give exact information on the neuromuscular status of the bladder. Constant drainage with an indwelling catheter or the use of "tidal drainage" (Munro⁵) is necessary if there is any urinary retention; it is often advisable in cases of reflex emptying of the bladder to prevent the frequent soiling of the bed and consequent maceration of the patient's skin.

Drainage of cerebrospinal fluid from the nose or ears is positive clinical proof of a basal skull fracture. Drainage of blood is suggestive, especially if from the ears. In the case of either, no effort should be made to obstruct it. The only exception to this is the occasional profuse nasal hemorrhage which may require a pack to control. This should not be left in longer than a few hours. Any irrigation or mechanical cleansing of the ear or nose is to be avoided. In the case of drainage from the nose, the patient if conscious is to be cautioned against sneezing or blowing his nose. A pad of cotton or gauze may be taped loosely against the ear or nose to collect draining fluid and removed as often as necessary. The patient should be kept flat until the drainage stops.

CONTROL OF INTRACRANIAL PRESSURE

Cerebral injury is inevitably associated with at least local edema. It often is associated with marked increase in intracranial pressure. If edema or swelling of the brain is generalized, the cerebrospinal fluid is squeezed out of the subarachnoid spaces and ventricles and the brain presents the appearance of the so-called dry brain of the pathologist. Obviously, in these cases an accurate index of intracranial pressure is difficult to obtain by manometric measurement of ventricular or lumbar fluid pressure, especially the latter.

There are three methods available for the control of intracranial pressure following acute brain injury. The first of these is control of the fluid intake. The surgeon must order the amount and type of fluids that a patient is to receive, and the nurses and house staff must see that he does receive it. Obviously, it is necessary that nurses keep an accurate record of the patient's intake. A record of output is of great value but often difficult to obtain accurately. We ordinarily limit fluid intake to from 1,200 to 1,500 cc. in twenty-four hours. Conscious patients, of course, take this by mouth. Unconscious patients or stuporous patients must receive fluids by other routes. The intravenous method is usually employed. As previously stated, we do not give saline solution unless positively indicated but prefer 5 or 10 per cent dextrose solution in distilled water. Patients who are comatose more than three days should have nasal feedings of a high caloric and high vitamin liquid diet. Nasal feedings also provide for administration of drugs or cathartics.

Dehydration of a patient may be actively accomplished, when indicated, by saline cathartics, saline enemas or the intravenous administration of hypertonic solutions. The first two are so well known as hardly to need comment, but it might be remarked that the rectal administration by the drip method of from 200 to 400 cc. of a 50 per cent solution of magnesium sulfate will often be as efficient in the reduction of increased intracranial pressure as the administration of 100 cc. of 50 per cent sucrose intravenously and will be a great deal less drastic from the standpoint of effect on the circulatory system.

The intravenous administration of hypertonic fluids is of great value in many cases of brain injury and is disappointing in orders. Obviously this method requires an intact local circulation in order for it to work and of course the local circulation is more or less impaired at the site of cerebral contusion or laceration. From 500 to 1,000 cc. of 10 per cent dextrose or from 200 to 400 cc. of 25 per cent sucrose or from 50 to 100 cc. of 50 per cent sucrose are the concentrations and amounts most frequently used. Fifty per cent sucrose is very strongly hypertonic and is to be used with corresponding caution.

Drainage of cerebrospinal fluid by spinal or ventricular tap is a method of treatment concerning which there has been a great deal of dispute. Again it is a method of great value in certain cases, disappointing in others and at times positively dangerous. The danger would seem to be principally that of producing a herniation of the cerebellar tonsils into the foramen magnum or of the hippocampal gyrus into the incisura tentorii because of marked increase in intracranial pressure and relatively low cerebrospinal fluid volume. Ventricular drainage, which is of such great value in certain cases of intracranial tumor, has had little trial in cases of

4. Voris, H. C., and Landes, H. E.: Cystometric Studies in Cases of Neurologic Disease, *Arch. Neurol. & Psychiat.* 44: 118-139 (July) 1940.

5. Munro, Donald: Craniocerebral Injuries: Their Diagnosis and Treatment, New York, Oxford University Press, 1938. Munro, Donald, and Hahn, Joseph: Tidal Drainage of the Urinary Bladder, *New England J. Med.* 212: 229-239 (Feb. 7) 1935.

brain injury. It certainly deserves further trial. Cisternal puncture will always be contraindicated where lumbar puncture is in cases of head injury. If there is danger of herniation at the foramen magnum, cisternal puncture is dangerous if not impossible because of the obliteration of the posterior cistern by the prolapsed cerebellum.

TABLE 3.—Results of Treatment by Cerebrospinal Fluid Drainage and Hypertonic Fluids

Treatment	Living	Dead	Total	Mortality Rate
Cerebrospinal fluid drainage alone..	37	8	45	17.8
Hypertonic fluids alone	145	86	231	37.2
Cerebrospinal fluid drainage and hypertonic fluid	67	35	102	34.4

Our attitude toward these methods can be best shown by the fact that of 1,394 patients only 231 were treated with intravenous administration of hypertonic solutions, with a mortality for the group of 37.2 per cent. Forty-five were treated with lumbar drainages (receiving at least two) with a mortality of 17.8 per cent. Another group of 102 patients received both forms of treatment with a mortality of 34.4 per cent (table 3). The mortality rate in these groups is not a fair criterion of the efficacy of the two methods, for these were selected cases and spinal drainage was not used on many of the desperately injured patients who did receive intravenous hypertonic solutions.

TREATMENT OF COMPLICATIONS

The treatment of complicated cases naturally resolves itself into the treatment of surgical and nonsurgical complications. In our present series of cases only a relatively small group (2.3 per cent) have been treated surgically. Table 4 presents a synopsis of this group. The mortality was high (50 per cent) and the post-mortem observations indicate that this is due to two factors, associated cerebral injury and pulmonary complications, the two often occurring in the same patient. One of us⁶ has recently published the results of operation in a series of subdural hematomas. In that series, as in the present one, the mortality was very high in the acute subdural hematomas, owing to the associated brain injury.

The indications for operative treatment may be briefly listed as (a) compound depressed skull fracture, (b) certain simple depressed fractures and (c) extracerebral hematomas. Patients with compound depressed skull fractures are to be operated on with débridement and primary suture within the first eight to ten hours if the condition of the patient permits. Otherwise the wounds are to be left open or loosely approximated and allowed to heal by secondary intention. The fracture then may be elevated as an elective procedure if this is indicated. Unfortunately, if the wound becomes infected in the presence of comminuted fragments of bone an osteomyelitis will usually result, and often meningitis or brain abscess.

The elevation of a simple depressed fracture is almost always an elective procedure and should be delayed until the patient is out of danger. Rarely it may produce local neurologic symptoms or more rarely increased intracranial pressure and require early elevation. Many

depressed fractures cause no symptoms and may be left alone. It is our practice to elevate those in the frontal region for cosmetic reasons and those near the motor area because of the frequency of post-traumatic epilepsy associated with depressed fracture.

Extracerebral hematoma, especially extradural, is of course an indication for operative intervention. We have already called attention to the futility of operating on the acute subdural hematoma, although occasionally a patient is benefited. It appears that subdural bleeding sufficient to produce a hematoma large enough to cause pressure symptoms is almost invariably associated with severe brain contusion or laceration. Chronic subdural hematoma develops slowly with a gradual onset of symptoms. Associated brain injury is usually slight and the patient has ample time to recover from it before evidence of his hematoma appears. The operative results are correspondingly good.

The diagnosis of an extradural hematoma in a typical (so called) case should be easy. This is due to the fact that there is no severe associated brain injury and therefore the classic "lucid interval" is present. Then too there is an uncomplicated development of localizing signs. Unfortunately, the "typical" cases are in the minority as associated brain injury of considerable severity is often present. Thus patients are stuporous or comatose from the onset and localizing neurologic signs due to brain injury may be present from the onset. Then too the development of localizing signs may be masked in whole or part by preexisting coma. Careful watch must be kept on all comatose or stuporous patients for the deepening of coma and the appearance of new localizing signs or of signs of increasing intracranial pressure. Since acute brain injury can and does often simulate the picture of a progressive lesion, an exploratory burr hole under local anesthesia must often be resorted to. Six (18.8 per cent) of our thirty-two patients who were operated on had no extracerebral hematoma but they did have brain contusion or laceration. One patient had a subcortical hematoma which was not found at operation. In the seventy-four necropsies performed, extradural hematoma was considered the principal cause of death by one of us (Kearns) in eight cases (10.8 per cent). Two of these

TABLE 4.—Patients Operated On

Conditions Found	Total	Living	Dead	Necropsies	Cerebral Laceration	Pulmonary Disease
Extradural hematoma..	3	1	2	2	2	0
Subdural hematoma.....	17	8	9	5	5	3
Acute.....	7	1	6	4	4	2
Chronic.....	10	7	3	1	1	1
Depressed skull fracture.	6	5	1	0	0	0
Cerebral contusion or laceration.....	6	2	4	2	1	1
Total.....	32	16	16	9	8	4

patients had been operated on (table 5), leaving six (8.1 per cent) unrecognized cases. This illustrates the frequency and difficulty of recognition of the atypical case.

We do not consider decompression to be of therapeutic value per se in cases of brain injury. First of all, no matter how skilfully performed it can only add to the trauma and edema already present. Secondly, it has been our observation in performing routine decompressions in cases of inoperable brain tumors that it requires several days to a week before adjustment of the intra-

6. Voris, H. C.: Diagnosis and Treatment of Subdural Hematomas, Proc. Inst. Med. Chicago 13: 129-130, 1940.

cranial contents to the decompression takes place and signs of clinical relief as cessation of headache and vomiting and recession of papilledema appear. Obviously, a therapeutic procedure offering such tardy relief will be of little value in the treatment of acute brain injury.

The most important nonsurgical complications that we have to deal with are meningitis, toxic psychosis, pneumonia and cardiovascular and renal disease.

The incidence of meningitis in this group was low: seven cases (0.5 per cent) with four deaths. This is of interest in conjunction with the fact that there were forty-one cases in the series with drainage of cerebrospinal fluid to the exterior from either nose, ears or a compound depressed skull fracture. In this connection it might also be noted that there were 703 cases of scalp laceration in the series; only nineteen (2.7 per cent) became infected. A number of these had been sutured elsewhere before admission to the Cook County Hospital. The new methods of chemotherapy have in our hands, as in others, greatly reduced both the incidence and the mortality of intracranial infection. There were no cases of brain abscess in this series.

Many of our patients are chronic alcoholic addicts. We have already referred to the large number of patients who had the odor of alcohol on their breath at the time of admission. Further, many of these patients

hope of financial compensation as a result of their injury. We do have patients with persistent headache, dizziness, easy fatigue or personality change but they are relatively rare compared with the number seen in private practice. We do not believe we can assume that our treatment is entirely responsible for this. It is our practice to insist on a minimum of two weeks of

TABLE 6.—*Mode of Injury*

	Number	Per Cent
Automobile.....	346	24.8
Assault.....	346	24.8
Fall.....	347	24.9
Miscellaneous.....	56	4.0
Unknown.....	299	21.5
Total.....	1,394	100.0

bed rest for all patients unconscious more than fifteen minutes, all patients who have bloody spinal fluid and all patients with roentgenographic or clinical evidence of fracture of the skull. In addition, patients with mild injury that complain of persistent headache or dizziness for more than three or four days after the injury are placed on a more strict regimen of fluid limitation with fluids limited to 1,000 cc. in twenty-four hours and daily saline catharsis. This seems to be of real value in preventing post-traumatic sequelae in this type of case. To be effective it must be carried out early after the injury. Cases seen later with the post-traumatic syndrome rarely respond to this management.

During 1939 there were 1,394 patients with head injury admitted to the neurosurgic service of the Cook County Hospital. Table 1 gives the results. The disabled group includes only those patients who left the hospital with a neurologic defect that was expected to be permanent. Table 2 shows the distribution of cases by decades with mortality rates. This table shows strikingly the importance of the age of the patient in determining his chances for recovery. Many other authors have commented on this.

Necropsies were performed by one of us (Kearns) in seventy-four cases, or 38.5 per cent of the deaths. Table 5 gives what was considered to be the principal cause of death in these cases. It has already been noted that in twenty-one cases (28.4 per cent) of the nec-

TABLE 5.—*Necropsies Performed in Seventy-Four Cases (38.5 per Cent of Total Deaths)*

Necropsy	Number	Per Cent
Extradural hematoma.....	8	10.8
Subdural hematoma.....	19	25.7
Cerebral laceration.....	26	35.1
Miscellaneous associated injuries or diseases	21	28.4
Without skull fracture.....	29	39.2
With skull fracture.....	45	60.8

were debilitated and chronically malnourished. As a consequence, the incidence of toxic psychosis was high. This condition when associated with head injury is exacerbated by dehydration of the patient. It is essential to push fluids on these patients and to give ample sedation. At times some sedatives, especially the barbiturates, have a toxic effect and may add to the confusion and delirium. When the vital centers (cardiovascular and respiratory) seem intact we may make an exception to our usual rule and use morphine as a sedative. It is also our impression that spinal drainages, especially when the fluid intake is kept high, are of value in treating these cases. Needless to say, they are performed only with the patients under ample sedation.

The incidence of pneumonia and cardiovascular, renal and other associated disease was high. Of seventy-four necropsies one of us (Kearns) considered the principal cause of death to be unrelated to the head injury in twenty-one cases, or 28.4 per cent (table 5).

PROPHYLAXIS AND TREATMENT OF SEQUELAE

Sequelae of course cannot be adequately considered in our present series. We hope at a later date to present from the records of our follow-up clinic a complete study of the late effects of the head injury in this group of patients. We would, however, call attention to the fact that ninety-one patients (6.5 per cent) suffered some degree of permanent loss of neurologic function. Another point worth emphasizing is the relative rarity of cases seen in the follow-up clinic with subjective post-traumatic symptoms. Most of our patients have no

TABLE 7.—*Seven Hundred and Ninety Patients with Associated Injuries*

Face.....	523
Extremities.....	321
Chest.....	132
Neck.....	37
Abdomen and pelvis.....	26
Spine.....	19
Spinal cord.....	3
Peripheral nerves.....	1

ropsies the principal cause of death was miscellaneous associated injury or disease. In a large group of cases (25.7 per cent) there were subdural hematomas. These were practically all of the so-called acute type. We have already called attention to the high operative mortality in acute subdural hematomas and to our belief that only the occasional case of this group should be treated surgically.

The mode of injury is of considerable interest in dealing with cases of head injury. Table 6 shows that our patients can be divided into four almost equal

groups, one injured by automobile accidents, another by some form of assault, another by falls and a fourth by miscellaneous or unknown causes. The high percentage injured by falls speaks for a high percentage of alcoholism and syncopal attacks; the high percentage injured by unknown causes includes a large group of critically injured persons who were picked up by the police and brought in without any history.

Seven hundred and ninety patients suffered associated injuries to other parts of the body, often multiple and most frequently the face, extremities and chest. Table 7 gives the detailed figures for the location of these injuries.

COMMENT

1. In this group of patients, age seemed a very important factor in determining survival.

2. Associated injury and disease are important factors in determining survival. This is especially true in the older age groups.

3. There was a comparatively low percentage of cases in which surgical operation was performed. In this group of cases acute subdural hematoma proved to have a high surgical mortality, and we believe that operation should be done only in the rare case of this group. Chronic subdural hematoma is a much more favorable lesion from the surgical standpoint and operation is always indicated in these cases.

4. Watchful conservatism gives the best results in the management of head injuries. Supportive treatment, enforcement of rest and careful nursing care and observation pay high dividends.

5. Special methods of reduction of intracranial pressure are of value in selected cases. Their routine use is to be condemned.

6. Approximately 40 per cent of patients dying of head injury have no demonstrable skull fracture at necropsy. This shows the absurdity of relying on the presence or absence of fracture of the skull in determining prognosis or treatment.

31 North State Street.

ABSTRACT OF DISCUSSION

DR. S. BERNARD WORTIS, New York: Drs. Voris, Verbruggen and Kearns have emphasized the problems of the complications and management of head injury. Our material of 1,000 cases at Bellevue Hospital (Wortis, S. B., and Kennedy, Foster: *Surg., Gynec. & Obst.* 55:365 [Sept.] 1932) is in agreement with their observations. One can only emphasize again the points which they brought out: 1. The mortality rate varies with age. In our group we found that children under 12 had a mortality rate about one-half that of adults over 60. 2. We found that in this city automobile accidents and falls were the commonest causes of head injury. 3. Roentgenograms gave positive evidence of skull fracture in only about half of the patients, so that one cannot depend alone on the skull x-ray examination for determining the degree of severity of any head injury. 4. Autopsies were performed on 380 of our patients, and of these we found skull fractures present in 97 per cent; we found gross brain laceration present in 92 per cent of our autopsy material, and a very low incidence of sepsis; suppurative meningitis in only fourteen cases, and brain abscess in only two cases. 5. Seventy per cent of the people with head injuries admitted to Bellevue Hospital had bleeding from the cranial orifices. 6. Eighty-five per cent of the patients showed clinical evidence of neurologic disturbance of brain function. Ten per cent showed papilledema, 10 per cent had peripheral facial palsy, and generalized convulsions were found in about 110 of the 1,000 patients. We performed skull operations on thirty-seven patients, and in this group the mortality rate was about 50 per cent, so that our

treatment has become, as the years go on, more and more conservative. One can only emphasize the fact that the more conservatively one treats these head injuries the more effective the results will be. I agree entirely with the authors' suggestion that no one method of treatment seems to be effective; one must vary one's treatment depending on the clinical observations. Some patients require hypertonic solutions for the reduction of intracranial pressure; other cases do not. Any simple single formula meant to apply to the treatment of all cases of head injury is a detrimental formula.

DR. DONALD MUNRO, Boston: This subject is important because, as one's experience increases with head injuries, it becomes apparent that some day it is going to be the duty of the general surgeon to care for the majority of them, leaving only the difficult ones to the specialists. This paper emphasizes the number of head injuries that occur and covers the first two years following the establishment of the authors' service. My experience has also been in a municipal hospital, but it covers ten years, so perhaps I may be allowed to comment adversely on some of the more important points. I should like to comment on the 38 per cent of autopsies that the authors have had. I have been so fortunate as to have had four out of five, or slightly more, of my head injury autopsies done for me by the medical examiner of Suffolk County. From those autopsies I have learned more about how to handle and diagnose these cases than from any other single factor. In their summary the authors do not classify compound fractures separately. My experience has been that there are a considerable number of compound fractures in any group of head injuries and that their presence materially influences the ultimate mortality and that therefore their segregation is imperative. I am interested in the small number of extradural and subdural hematomas that they have had. I have had about 2,000 cases in the ten years as compared with their 1,300 in one year. In those 2,000 cases I had over forty-four extradural hematomas, as proved by either operation or autopsy. In that same group I had about 300 subdural hematomas. I do not think that there is any reason to differentiate between the acute and the chronic subdural hematomas. After all, every chronic hematoma is acute at its start. Since the chronic stage necessarily carries a lower mortality such a division gives false figures relative to the efficacy of any therapy, I feel strongly that subdural hematomas should be operated on early, and I always feel bad when the medical examiner finds in one of my cases a subdural hematoma that I have not had a chance to treat. In the first 225 of the 300 subdural hematomas that I experienced my operative mortality was 34 per cent. The most important point of difference between myself and the authors has to do with diagnosis. I don't believe that we shall ever get anywhere in learning about this subject until we base our classification of these cases on some universally recognized diagnosis.

DR. JOHN P. STUMP, New York: This paper makes the point that the report of the authors is based on cases of injury not only to the cranium and its contents but also to the rest of the body. Injuries to parts other than the head are important. Many reports have come from services that got their patients late or received patients with head injuries only. At Gouverneur Hospital in New York the patients with head injuries are admitted to the fracture and orthopedic service. They are seen almost simultaneously by a member of the fracture and orthopedic staff and a neurosurgeon. The neurosurgeons are not regarded as consultants, nor are we; we both participate in the treatment of these patients. We have recently reviewed the cause of death of patients having proved cranial or intracranial injuries, and of these approximately 20 per cent died of their head injuries alone, while 30 per cent of the patients who died had mortal body injuries and very slight intracranial injuries. The point I make is the importance of considering injury to the rest of the body, as well as to the head, as a potential cause of death.

DR. HAROLD C. VORIS, Chicago: I too wish we had more necropsies. We are thankful for the ones that we do have, which we owe to the cooperation of Dr. Kearns, the coroner's physician. The absence of skull fracture in from 35 to 40 per cent

of patients dying from head injury is based not only on this series but also on a much larger series collected by Dr. Kearns during previous years in the coroner's laboratory. It is therefore surprising that Dr. Wortis could demonstrate skull fractures in 97 per cent of necropsies in his series. In classification of cases, one can of course by proper selection make a mortality rate as high or as low within certain limits as wished. Therefore, in this preliminary paper we have reported our first year's experience, not with any particular type of head injury, but with the management of all cases of head injury admitted to a large neurosurgical service. I must defend the clinical classification of cases at the time of admission. I agree with Dr. Munro that in the end we must attempt to classify the patient according to the brain injury which we could or thought we could demonstrate. We have already pointed out that to begin with that is often not possible. If one attempts it one often has to change one's opinion within a short time. So from the standpoint of treatment and of early management the clinical grouping mentioned is most satisfactory. I wish we could report the results in acute subdural hematoma that Dr. Munro has. Frankly, our experience with acute subdural hematoma has not been sufficiently good to warrant our continuing to operate on these patients. I agree that there is no need to differentiate the cases preoperatively from extradural hematomas, and, whenever the latter is suspected, exploration should be made. On the other hand, although acute subdural hematomas represent the first stage of a possible chronic subdural hematoma, it is important to differentiate them clinically. The acute subdural hematoma is a large collection of blood without neomembranes, practically always associated with acute brain injury and with a high mortality. The chronic subdural hematoma was originally small and has neomembranes, the patient has recovered from his brain injury and the mortality is correspondingly low.

NEUROGENIC FACTORS IN THE PRODUCTION OF ACUTE GASTRIC ULCER

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Study of fifteen cases of acute gastric ulceration associated with primary intracerebral disease shows no essential pathologic difference between these lesions and the acute gastric ulcer found in the absence of such disease. That the mucosal lesion is the result of an acute phase of gastric circulatory deficiency of a prolonged type is suggested by the presence of chronic degenerative changes in the deeper layers of the stomach wall. Moreover, similar degenerative changes dependent on chronic stasis in the circulatory beds found in other viscera in these cases demonstrate that the so-called "neurogenic" ulcer is not a primary, isolated phenomenon but a focal manifestation of subclinical generalized circulatory insufficiency.

The absence of organic cardiovascular disease in this series, with a mean age of 34 years, permits the assumption that the generalized peripheral circulatory disturbances noted in the viscera mentioned are primarily related to an intracerebral condition. The nature of the pathologic alterations in the viscera suggests that the stasis in the peripheral circulation develops from prolonged vasoconstriction due to stimulation of the cerebral vegetative centers by the primary intracranial

disease. Assumption of a relationship between the peripheral circulatory abnormalities, the gastric lesion and central vegetative stimulation is based not only on the demonstrated pathologic alterations in the viscera

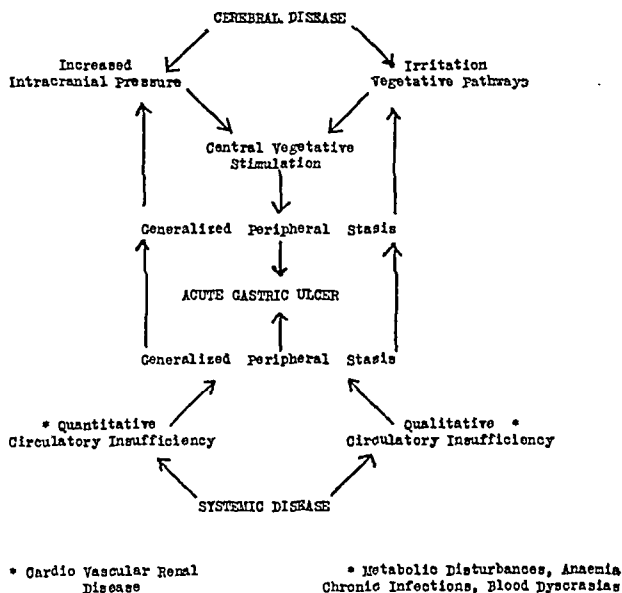


Fig. 1.—Mechanism of acute gastric ulcer.

mentioned but on the location and nature of the cerebral lesion (table 1).

In the cases we are presenting, stimulation of the central vegetative nuclei resulted either from increased intracranial pressure from tumor or abscess within the cranial cavity, or from irritation due to a focal lesion of the central vegetative pathways.

Destruction of the central vegetative nuclei was not an etiologic factor in these "neurogenic" ulcers. In ten cases of expanding new growths associated with acute ulcer it is believed that the ulcer was the direct result of stimulation of the hypothalamic centers from increased intracranial pressure rather than destruction of the centers by the cerebral lesion itself. This is well illustrated by the four cases of tumor involving the



Fig. 2.—Systemic circulatory disturbances in primary intracerebral disease: Section of stomach of a person, aged 29, with primary brain tumor. Focal area of acute ischemic necrosis involving entire depth of mucosa. Chronic stasis in deeper layers with resulting fibrosis and atrophy. Trichrome stain.¹ Reduced from a photomicrograph with a magnification of 57 diameters.

hypothalamic centers. Here the centers were affected by compression of the blood supply rather than by actual invasion of the tissue. On the other hand, the five cases not associated with increased intracranial

From the Divisions of Medicine and Neuropathology, Philadelphia General Hospital.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Beyer, E. M.: Trichrome Stain for Astrocytes, *Am. J. Clin. Path.* 10: 65-68 (May) 1940.

pressure, while involving the vegetative areas, were essentially characterized by lesions which would result in irritation rather than destruction.

Thus, in this series of "neurogenic" ulcers it is possible to demonstrate a central etiologic factor, namely



Fig. 3.—Systemic circulatory disturbances in primary intracerebral disease: Section of heart of a person, aged 29, with primary brain tumor. Venous channels are greatly dilated. There is interstitial edema. There is increased perivascular connective tissue around both arteries and veins. (Section taken from the apex of left ventricle.) Trichrome stain.¹ Reduced from a photomicrograph with a magnification of 71 diameters.

blood supply; however, excessive stimulation of this physiologic mechanism may result in anoxia of tissues and later in increased capillary permeability, tissue edema and decreased circulating blood volume. Tissue edema, thus established, augments the irritability of the cerebral centers through the mechanism of asphyxia and, because of its demyelinating effects on peripheral nerve pathways, may render the entire vegetative system sensitive to subminimal stimuli. In turn, the vasoconstriction of vessels resulting from abnormal neural irritability aggravates the preexisting stasis.



Fig. 5.—Systemic circulatory disturbances in primary intracerebral disease: Section of kidney of a person, aged 29, with primary brain tumor. There is marked increase of perivascular connective tissue. There is thickening of Bowman's capsule and hyalinization of the glomerular capillary tufts. Trichrome stain.¹ Reduced from a photomicrograph with a magnification of 92 diameters.

stimulation of the central vegetative mechanism, which in turn causes the stasis or vasoconstriction responsible for the ulcer. While emphasis has been placed on the role of changes in the peripheral circulation due to stimulation of the sympathetic system in the production of ulcer, we appreciate that parasympathetic stimulation must be considered because of similar demonstrable pathologic alterations in this system.

While the intracranial lesion is the immediate factor initiating cerebral vegetative activity, the stimulating

TABLE 1.—Acute Gastric Ulceration in Primary Cerebral Lesions in Fifteen Cases

Location	Cerebral Lesion	Cerebral Vegetative Involvement	
		Increased Intracranial Pressure	Focal Lesion Vegetative Pathways
Hippocampus.....	Glioma	+	+
Basal ganglions.....	Glioma	+	+
Pituitary.....	Adenoma	+	+
Infundibulum.....	Adamantinoma	+	+
Parietal.....	Glioma	+	0
Parietal.....	Glioma	+	0
Parietal.....	Meningioma	+	0
Temporal.....	Abscess	+	0
Temporal.....	Glioma	+	0
Cerebellum.....	Abscess	+	0
Periventricular gray matter.....	Multiple sclerosis	0	+
Periventricular gray matter.....	Multiple sclerosis	0	+
Periventricular gray matter.....	Traumatic encephalopathy	0	+
Hypothalamus; basal ganglions	Paresis	0	+
Hypothalamus; basal ganglions	Paresis	0	+



Fig. 4.—Systemic circulatory disturbances in primary intracerebral disease: Section of liver of a person, aged 29, with primary brain tumor. Increased interstitial connective tissue. Dilatation of liver sinusoids. Degenerative changes in liver cells with accumulation of lipid. Trichrome stain.¹ Reduced from a photomicrograph with a magnification of 230 diameters.

effects of the resulting peripheral circulatory disturbances on the vegetative system itself may establish a vicious cycle. Normally, peripheral vasoconstriction due to central vegetative control insures adequate cerebral

On this premise the basic mechanisms underlying acute gastric ulcer associated with intracranial disease, and ulcer unassociated with such disease, differ only in the nature of the primary factor responsible for the circulatory insufficiency. In "neurogenic" ulcer the pressor effect of central vegetative stimulation by the intracranial lesion initiates the peripheral stasis; in other forms of acute focal gastric lesion the same end result is produced by quantitative or qualitative alterations in the general circulation.

Although it is possible to distinguish neurogenic and visceral factors initiating the peripheral circulatory imbalance which we believe underlies acute gastric ulceration, the blood stasis resulting from such imbalance by its effect on the nervous system establishes a secondary neural cause for all such lesions regardless of

TABLE 2.—Acute Gastric Ulcer: Etiology of Central Vegetative Stimulation in Primary Systemic Disease

Increased intracranial pressure.....	67 cases
Massive cerebral vascular lesion.....	29
Brain edema.....	36
Lead encephalopathy.....	2
Focal lesions, central vegetative pathways.....	26 cases
Periventricular gray matter.....	9
Hypothalamus.....	2
Thalamus.....	4
Midbrain.....	2
Medulla.....	4
Spinal cord.....	5

TABLE 3.—Relation of Central Vegetative Stimulation to Acute Ulcer in Primary Systemic Disease, 143 Cases

Cerebral Complications	Cases	Ulcer
Increased intracranial pressure.....	78	67
Focal lesion, central vegetative pathways.....	31	26
No cerebral complications.....	34	20

the primary etiologic factor. In some cases in which the gastric lesion is not associated with intracranial disease, the influence of this neural factor alone may be sufficient to produce acute gastric ulceration. Generally speaking, however, central vegetative stimulation

cerebral disease (table 2); in ulcers unassociated with intracerebral disease, these same stimulating factors are established by deficiencies in the cerebral circulation resulting from the generalized circulatory insufficiency accompanying systemic disease.

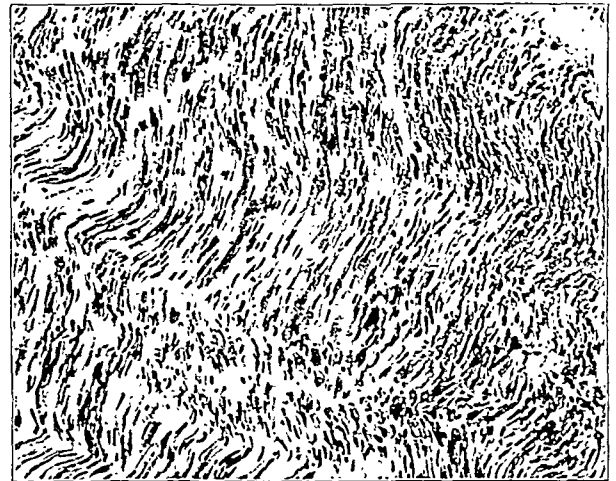


Fig. 7.—Alterations in peripheral vegetative system in primary intracerebral disease: Section of vagus nerve (intrathoracic portion) of a person, aged 27, with primary brain tumor. Nerve fibers separated by edema. Patchy demyelination with generalized increase in interstitial elements. The remaining myelin sheaths are swollen and vacuolated. Weil myelin sheath stain. Reduced from a photomicrograph with a magnification of 149 diameters.

The influence of central vegetative stimulation in bringing about circulatory insufficiency in systemic disease, thereby precipitating acute gastric ulcer, is demonstrated in table 3. In systemic disease, 82 per cent of the cases with ulcer presented evidence of increased intracranial pressure or changes in the central vegetative pathways which were secondary to the cerebral effects of peripheral circulatory insufficiency. Furthermore, ulceration occurred four times more frequently in cases of primary systemic disease with secondary central vegetative stimulation than in those without such stimulation of the central nervous system.

CONCLUSIONS

- 1. "Neurogenic" ulcer is a focal expression of sub-clinical generalized circulatory insufficiency, initiated through stimulation of the central vegetative mechanism by primary intracerebral disease.
- 2. In the absence of primary intracerebral disease, changes in the vegetative nervous system resulting from circulatory insufficiency may exert a neurogenic influence in ulcer production.

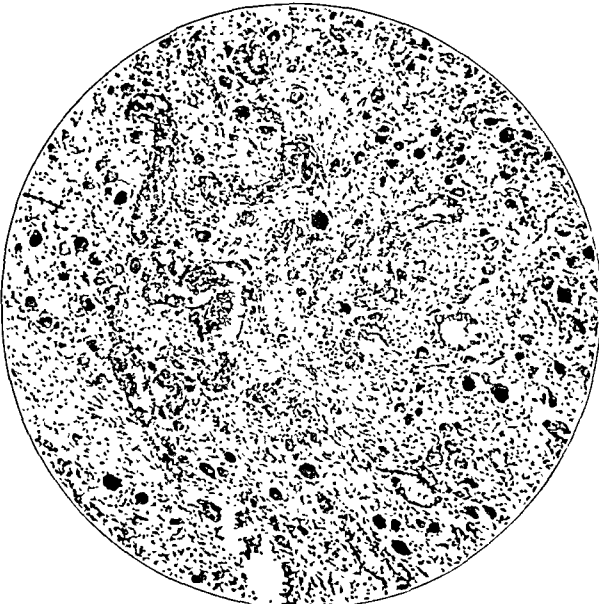


Fig. 6.—Alterations in peripheral vegetative system in primary intracerebral disease. Section of lumbar sympathetic ganglion (vertebral chain) of a person, aged 27, with primary brain tumor. Intense stasis. Loss of ganglion cells. Remaining cells show ischemic degeneration. Marked increase in interstitial tissue. Trichrome stain.¹ Reduced from a photomicrograph with a magnification of 69 diameters.

appears to be the predominant factor in the production of acute gastric ulceration whether it is of the non-neurogenic or the neurogenic type. In "neurogenic" ulcer the factors responsible for such central stimulation (namely increased intracranial pressure or lesions of the vegetative pathways) are due to the primary intra-

Functional Murmurs.—Potain made the most exhaustive study of functional murmurs. He found such murmurs present in one eighth of all the patients seen in his hospital service. They were present in practically all of the cases of Graves' disease, in 50 per cent of the cases of chlorosis, 25 per cent in measles and scarlet fever, 10 per cent in pulmonary disease. . . . The student should not gain the impression that functional murmurs are truly "accidental" and to be altogether disregarded. Often they may, quite often they may not, be disregarded. A relative insufficiency of the mitral valve due to an enlarged left ventricle produces a systolic murmur which is functional so far as there is no organic pathological process on the mitral leaflets. Such a murmur, however, may be of as great as or greater importance than the systolic organic murmur of an almost perfectly functioning mitral valve.—Major, Ralph H.: Physical Diagnosis, Philadelphia, W. B. Saunders Company, 1940.

FATAL HEMORRHAGE FROM
PEPTIC ULCERONE HUNDRED AND SIXTEEN CASES COLLECTED
FROM VITAL STATISTICS OF SEATTLE DURING
THE YEARS 1935-1939 INCLUSIVE

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AND

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SEATTLE

The mortality risk of hemorrhage from peptic ulcer has been reported by various observers¹ as varying from a fraction of 1 per cent to as high as 74 per cent, the last figure reported by Chiesman² in a selected group of recurring hemorrhages. Allen³ and Blackford and Cole⁴ reported simultaneously (1937) that in older persons having massive exsanguinating hemorrhage the mortality rate approximated 30 per cent in their hospital practice and that age was the greatest factor influencing mortality.

Recent reports of mortality rates of from 1 to 2 per cent for hemorrhage from peptic ulcer when under special medical treatments have been made by Meulengracht,⁵ Andreson⁶ and others; and Hurst⁷ feels that a death in private practice from hemorrhage from ulcer is rare. On the other hand, Hinton,⁸ Goldman,⁹ Crohn¹⁰ and many others report higher mortality rates, often much higher.

The wide variation in mortality statistics must be due to a difference in the type of cases included for study by the various authors. Most reports include all cases admitted to the hospital for gross hemorrhage, regardless of age or the seriousness of the hemorrhage. Some medical men have excluded surgical deaths from their statistics. Many reports include patients bleeding from marginal ulceration. No report includes the mortality outside of hospitals.

Last year Blackford and Cole⁴ reported all deaths during two years considered due to hemorrhage from peptic ulcer, as recorded by the Seattle Bureau of Vital Statistics, together with their clinical experiences with hemorrhage from peptic ulcer. Gross hemorrhage from ulcer was defined as that evidenced by hematemesis or melena without regard to clinical symptoms, and massive hemorrhage as gross hemorrhage with great loss of blood plus critical symptoms of acute anemia. It was noted that early blood determination gave little or no information that was of value. Only 40 per cent of all first hemorrhages in the series occurred in patients past 45 years of age. Half of the hemorrhages in older patients were massive hemorrhages.

From the Mason Clinic.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Lynch, R.: *Canad. M. A. J.* 17: 677-681 (June) 1927. Ross, K.: *M. J. Australia* 1: 163-170 (Feb. 8) 1930. Aitken, R. S.: *Lancet* 1: 839-842 (April 21) 1934. Helliier, F. F.: *ibid.* 2: 1271-1274 (Dec. 8) 1934. Hinton, J. W.: *Ann. Surg.* 101: 856-862 (March) 1935. Goldman, Leon: *Am. J. Surg.* 40: 545-551 (June) 1938. Graham, J. G.: *Alexander, J. C., and Kerr, J. D. Olav.: Lancet* 2: 727-729 (Sept. 30) 1939. Chiesman,² Allen and Benedict,¹² Goldman,⁹ Allen,³ Crohn and Lerner,¹⁰ Blackford and Cole.⁴ Meulengracht.⁵
2. Chiesman, W. E.: *Lancet* 2: 722-723 (Oct. 1) 1932.
3. Allen, A. W.: *Surgery* 2: 713-731 (Nov.) 1937.
4. Blackford, J. M., and Cole, W. S.: *Am. J. Digest. Dis. & Nutrition* 6: 637-641 (Nov.) 1939.
5. Meulengracht, E.: *Brit. M. J.* 2: 320-324 (Aug. 12) 1939.
6. Andreson, A. F. R.: *Am. J. Digest. Dis. & Nutrition* 6: 641-646 (Nov.) 1939.
7. Hurst, A. F.: *Guy's Hosp. Rep.* 86: 129 (March) 1936.
8. Hinton, J. W.: *Am. J. Surg.* 33: 180-182 (Aug.) 1936.
9. Goldman, Leon: *Gross Hemorrhage from Peptic Ulcer*, J. A. M. A. 107: 1537-1542 (Nov. 7) 1936.
10. Crohn, B. B., and Lerner, H. H.: *Am. J. Digest. Dis. & Nutrition* 6: 15-22 (March) 1939.

VITAL STATISTICS

We now present all deaths recorded with the Seattle Bureau of Vital Statistics during the five years 1935-1939 inclusive in which it seems reasonably certain that the patient died as the result of hemorrhage from peptic ulcer. Death due to hemorrhage from peptic ulcer is so startling an event that the physician should not fail to note the hemorrhage on the death certificate; for this reason, the list should be fairly complete.

These cases have been collected as follows: All death certificates (23,955) were reviewed individually, and each certificate on which the fatality was attributed to hemorrhage from peptic ulcer was listed for study. The cross index of vital statistics was not relied on because of the chance of clerical error; and some errors were found for the two years previously reported.⁴ All cases were traced back to hospital records, to the physician who signed the certificate or to the family of the deceased. One coroner's case could not be traced.

The list includes all cases in which death was apparently properly attributed to hemorrhage from peptic ulcer. The tracing back to clinical records allowed the elimination of a few cases which we felt should not be included, particularly (1) bleeding from gastroduodenal or marginal ulceration, (2) sudden fatal gastric hemor-

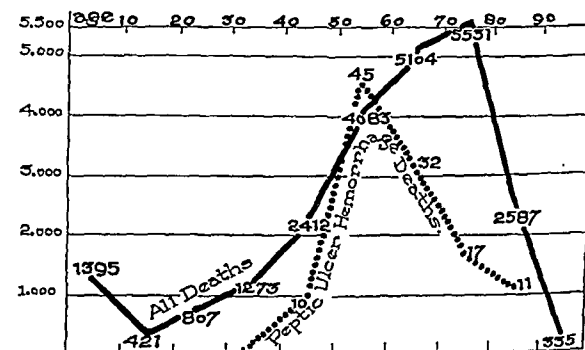


Chart 1.—Distribution of 116 deaths from peptic ulcer hemorrhage among 23,964 deaths.

rhage which was the only evidence of ulcer, (3) acute hemorrhagic gastritis and (4) gastric hemorrhage which was manifestly not the immediate cause of death.

The records of ninety-seven men and nineteen women, or 116 cases in all, have been thus collected as representing all deaths in Seattle during five years which were considered due to hemorrhage from peptic ulcer. Exactly half of these, fifty-eight, were confirmed by autopsy as death due to hemorrhage from ulcer. The high percentage of autopsies is due to the fact that most deaths reported were in hospitals with active post-mortem services and with competent pathologists in charge.

Autopsy records of these fifty-eight cases show that the hemorrhage was from gastric ulcer in thirty-seven and duodenal ulcer in seventeen, and that the location of the ulcer was not stated in four. Arteriosclerosis was recorded repeatedly on the death certificate as a contributing cause of death, as determined by autopsy.

Deaths attributed to hemorrhage from peptic ulcer but not studied by autopsy are, of course, not proved to be deaths due to hemorrhage from peptic ulcer. These cases were, however, so certified by the physician in charge. It is usually considered that approximately 90 per cent of gross gastric hemorrhages are hemorrhages from peptic ulcer. If we assume that only

80 per cent of clinical diagnoses not studied by autopsy are correct and that all the diagnoses confirmed by autopsy are correct, then the diagnosis of death due to hemorrhage from peptic ulcer should be correct in more than 90 per cent of these 116 cases.

Chart 1 shows by decades the total number of deaths in Seattle during five years and a superimposed curve shows the total number of deaths from hemorrhage from peptic ulcer during these years. It is evident that the great majority of deaths occurred between the ages of 50 and 70 years. Only three individuals were under 45. Their ages were recorded as 39, 42 and 43.

Chart 2 shows where these patients died: 22 per cent of them (twenty-six cases with eleven autopsies) at home—a group of fatalities never included previously in any clinical statistics on this subject; fifteen of the twenty-six patients dying at home were past 70 years of age. Sixty per cent of hospital mortality occurred in private general hospitals; and the private general hospitals in Seattle carry 66 per cent of the general hospital occupancy.¹¹

Almost all fatalities (97+ per cent) occurred in patients past 45 years of age, and less than 3 per cent were of persons under 45 years.

Most dramatic is the fact that 78 per cent of all fatalities (ninety cases) occurred following the first hemorrhage; only 22 per cent of all patients dying of hemorrhage from peptic ulcer (twenty-six cases) gave a history of previous hemorrhage.

Twelve patients who died had been operated on for emergency control of bleeding. One was operated on within forty-eight hours of the onset of hemorrhage and died of peritonitis on the tenth day; eleven were operated on from three to eleven days after the onset of massive hemorrhage.

Emergency operation on older patients in the first forty-eight hours of critical bleeding has rarely been undertaken in this country. We have found no report of a series of such cases. Later operation (after forty-eight hours) in critical cases has been followed by very high mortality rates.

Emergency operations in Seattle for hemorrhage from peptic ulcer are unusual. This is evidenced by the fact that not more than one surgical fatality has occurred during five years in any private hospital in Seattle and that two of the private hospitals have had no post-operative deaths. At the King County Hospital, six fatalities have followed the work of six different operators. No Seattle surgeon has had more than one death. Yet the city of Seattle has averaged two deaths each month from hemorrhage from peptic ulcer, and two thirds of those patients who died were under 70 years of age and were admitted to hospitals.

CLINICAL IMPRESSIONS

The clinical study of last year emphasized that, although 60 per cent of first hemorrhages from peptic ulcer occur in patients under 45 years of age, fatalities from hemorrhage are almost unknown in patients aged less than 45 years. The present study of the total mortality experience with hemorrhage from peptic ulcer taken from the vital statistics of a city of nearly 400,000 people shows how true that statement is.

The risk to life of hemorrhage from ulcer in younger patients is manifestly a small fraction of 1 per cent and the risk does not exceed 1 per cent even if only massive exsanguinating hemorrhages are considered. Therefore

one is rarely, if ever, justified in attempting to select those younger patients who are likely to die from hemorrhage from ulcer in order to consider operation as necessary to save their lives. No surgical procedure under such circumstances carries a risk of less than 1 per cent.

We have also pointed out that critical massive hemorrhage in older patients carries a mortality rate approximating 30 per cent, confirming Allen's report.¹² We also noted that five of our six fatalities followed the first hemorrhage. Allen³ reported 60 per cent of fatalities as following the first hemorrhage. It is usually taught that risk to life increases with each succeeding massive hemorrhage; yet three fourths of all fatalities reported in Seattle followed the first hemorrhage. It therefore seems certain that the first massive hemorrhage in older people is by far the most dangerous hemorrhage, a fact quite at variance with clinical impressions.

Surgeons have often remarked that risk to life increases with each recurring hemorrhage from ulcer; they have overlooked the fact that the mortality of all subsequent hemorrhages represents only about one fourth of the total mortality from bleeding ulcer. Three fourths of all deaths occur following the first hemor-

HOSPITALS	age 40	45	50	60	70	75	80
37 County	1	2	13	12	2	4	3
15 Swedish		1	7	3	2	1	1
8 Providence	1	1	5	1			
10 Marine	1	1	4	4			
5 Seattle General		1	2	2			
5 Columbus			4	1			
3 Virginia Mason		1	1	1			
2 Maynard			1	1			
5 Others			1	4			
26 Home		1	7	3	3	5	7
116 Total	1	2	8	45	32	7	11

• = operated

Chart 2.—Deaths from peptic ulcer hemorrhage.

rhage; only one fourth of all patients dying from ulcer hemorrhage have lived through a first hemorrhage to die later from another hemorrhage.

Such is the challenge of vital statistics for a reduction in the mortality of older patients. Bleeding from the ruptured, spurting, arteriosclerotic artery is apparently uncontrollable in one third of the cases of massive hemorrhage from ulcer in older people, unless it can be controlled by surgical intervention.

Occasionally, death from exsanguination occurs so quickly that there is no chance for any kind of intervention. Some patients are seen so late that operation is a last resort, and usually a forlorn hope, for life saving. Some patients are so handicapped by age or other infirmities that any surgical procedure is hardly to be considered. Still, the majority of these 116 patients whose bleeding resulted fatally were admitted promptly to hospitals and died from exsanguination a number of days later.

SURGICAL INDICATIONS

Finsterer,¹³ Gordon-Taylor,¹⁴ Hinton,⁸ Pfeiffer¹⁵ and many others believe that prompt operative intervention

12. Allen, A. W., and Benedict, E. B.: *Ann. Surg.* 98: 736-749 (Oct.) 1933.

13. Finsterer, H.: *Surg., Gynec. & Obst.* 69: 291-298 (Sept.) 1939.

14. Gordon-Taylor, Gordon: *Lancet* 2: 811-815 (Oct. 12) 1935.

15. Pfeiffer, D. B.: *Gastric Hemorrhage*, *J. A. M. A.* 111: 2198-2201 (Dec. 10) 1938.

should save many lives. Their reports give reason to hope that the record for critical hemorrhage in older people may be greatly improved by operation within the first forty-eight hours. After that time there is abundant evidence of terrific mortality following surgical intervention. It seems that tissue changes and bone marrow exhaustion after forty-eight hours of exsanguination make recovery from the shock of operation an unusual event.

Published reports of operative cases to date are, however, inconclusive in that patients operated on have not been grouped according to age. Many such operations have been done on younger patients. From the evidence of our clinical records, together with the evidence of vital statistics, the mortality risk of critical hemorrhage in younger patients is less than 1 per cent; hence operative intervention in such cases should actually increase the risk to life. In fact, we know of no surgical experience that justifies emergency operation for hemorrhage from ulcer in younger patients, even with prostrating hemorrhage. Less than 1 per cent will die if not operated on.

Forty-five years seems to be the age past which the risk of death from hemorrhage increases rapidly. In fact, nearly all fatalities are included in the group of older patients having critical hemorrhages from ulcer, and three fourths die following the first hemorrhage. The mortality rate would be well above 30 per cent in this group if all the massive hemorrhages shown in vital statistics could be included.

Operations done after unsuccessful attempts at supportive treatment through days of bleeding have usually resulted fatally. Eleven of the twelve patients cited as operated on in our vital statistics were operated on from three to eleven days after the onset of massive hemorrhage. Delayed operation at the Massachusetts General Hospital resulted fatally in 100 per cent of the cases.¹² All experience seems to show that operations done after several days of massive bleeding are followed by terrific mortality.

Prompt surgical intervention for critical bleeding from ulcer in older patients seems to offer the only hope of reducing the present mortality rate, which is above 30 per cent. An actual reduction in present surgical mortality should be accomplished by excluding younger patients from operation even when they are suffering critical hemorrhage from ulcer.

SUMMARY

All consecutive fatalities from hemorrhage from peptic ulcer during five years in Seattle show that:

1. Ninety-seven + per cent occurred in patients past 45 years of age.
2. Seventy-eight per cent died following the first hemorrhage.
3. Twenty-two per cent died at home.
4. Sixteen per cent were women.
5. Only twelve patients who died were operated on, each by a different surgeon.
6. Eleven of the twelve were operated on more than forty-eight hours after the beginning of hemorrhage.
7. Autopsy studies show more deaths from hemorrhage from gastric ulcer than from duodenal ulcer.

CONCLUSIONS

The vital statistics of Seattle show a remarkable number of deaths from massive hemorrhage from peptic ulcer in patients past 45 years of age, as contrasted with the very few deaths in those under 45. Three

fourths of all deaths resulted from the first hemorrhage. Prompt surgical control of massive hemorrhage seems to be the only hope of saving the lives of one third of the older patients having massive hemorrhage from peptic ulcer. This study gives further confirmation of the great risk of operations done after forty-eight hours of massive bleeding from ulcer.

Virginia Mason Hospital Building.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRs. BOLES AND RIGGS AND
DRs. BLACKFORD AND WILLIAMS

DR. WALTER L. PALMER, Chicago: Drs. Boles and Riggs have shown pathologic alterations in the viscera other than the stomach in fifteen cases of acute gastric ulceration associated with primary intracerebral disease. These lesions may be due to circulatory disturbances. It would be interesting to know whether similar changes were found in patients dying of causes other than intracerebral disease and whether the changes were found both with and without gastric ulceration. The possibility that the lesions may be the result of the complex processes of death, of so-called agonal changes, does not seem to me to be excluded by the histologic evidence offered; in fact, acute gastrointestinal ulceration is seen not infrequently both in man and in the experimental animal in death from various causes. Perhaps such ulcerations are due to peripheral circulatory changes occurring in the last hours of life and perhaps the central nervous system does play a role in these circulatory changes. These assumptions, however, seem to be by no means proved; however, even if they are true they do not seem to warrant the further assumption that "the central vegetative mechanism has an important part either as a primary factor or a neurogenic complication in the etiology of acute gastric ulcer." Would it not be more appropriate to reverse the reasoning and to look on the ulcer as an incidental result or a localized manifestation of the complex processes leading to the death of the organism, which in these cases happened to be initiated by intracerebral disease? Drs. Blackford and Williams have approached the subject of massive hemorrhage from a new point of view and obtained results which emphasize still further the importance of this complication of peptic ulcer. I am impressed particularly with the seriousness of the first hemorrhage. Dr. Kirsner and I last year reviewed our cases of massive hemorrhage and found that five of eight deaths occurred in the first hemorrhage. We found that 1.8 per cent of our patients, numbering 165, under 50 years of age died, whereas the mortality rate of patients over 50 years of age was 7.6 per cent. It may be that surgery is indicated in this age group; however, at present, and under the circumstances obtaining in massive hemorrhage, I doubt that the surgical mortality rate will be found to be less than the 7.6 per cent obtained in our series with medical treatment.

DR. SIDNEY LEIBOWITZ, New York: These remarks are based on studies of Dr. Chasnoff and myself and express our combined opinions. We wish to compliment Drs. Blackford and Williams on their unique approach to the problem and their careful analysis of such material. The value of this study is enhanced by the fact that so large a percentage of the cases at autopsy proved to be instances of hemorrhage from ulcer. Our experience is based on studies of clinical material rather than fatalities alone. It has repeatedly been stressed that a large proportion of the fatal cases of ulcer hemorrhage occur in the arteriosclerotic age group. Yet to hear this figure placed at 97 per cent is unusual. In our own small series of ninety-three patients nine deaths occurred, of which five (55 per cent) were of patients older than 45. Equally surprising is the report that 78 per cent of the fatalities occurred after the initial hemorrhage. This finding is contrary to the prevailing impression and will undoubtedly alter our concept of the gravity of initial hemorrhage. We have no doubt that an earnest effort was made to check the possibility of previous hemorrhage, but it is conceivable that some

of these patients may have had previous episodes of bleeding not revealed in their histories. We examined our own cases from this standpoint and were surprised to find that as many as 55 per cent gave no previous history of hemorrhage. Let us accept the statistical conclusions arrived at by the authors. If, in addition, we assume that early operative intervention in the older group is attended by a mortality appreciably less than the 30 per cent apparently obtained with medical treatment in this group, we must inevitably conclude that massive first hemorrhage in older individuals demands immediate surgery. We are reluctant to follow this reasoning to such a conclusion. The patient's age and the fact that it is his first bleeding episode are insufficient indications, in any one case, that death will ensue. The problem still remains to determine early which patients are likely to die. We feel that there are no satisfactory early criteria. By the time the clinical picture indicates the probable fatal outcome, it is usually too late for successful surgery.

DR. IRVING GRAY, Brooklyn: In 1931 Cushing reported that following the injection of solution of posterior pituitary and pilocarpine into the lateral ventricle in man there was increase in gastric tonus, hypermotility and hypersecretion. The following year he reported a series of cases in which there occurred acute perforation of the esophagus, stomach and duodenum responsible for death from one to four days after operation on the brain for the removal of tumors. He presented evidence in support of the existence of a parasympathetic center in the hypothalamus which sends fibers to the medullary vagus center. Beattie, Masten and Bunts, Keller, and Holler and Pollack have made contributions which point to the existence of a parasympathetic center situated in the hypothalamus which sends impulses downward to the medullary vagus centers. Drs. Boles and Riggs have pointed out that the acute gastric ulceration in their series shows (1) no essential pathologic difference between these lesions and the acute gastric ulcer found in the absence of such disease, that (2) the mucosa lesion is the result of an acute phase of gastric circulatory deficiency of a prolonged type and that (3) pathologic alterations in other viscera in these cases demonstrate that the so-called neurogenic ulcer is not a primary isolated phenomenon but a focal manifestation of a generalized circulatory insufficiency. In view of these observations, which indicate that the so-called neurogenic ulcer is not an isolated phenomenon in the stomach but an expression of generalized circulatory insufficiency, it might be reasonably assumed that a variety of cerebral pathologic conditions may lead to the production of focal areas of vascular disturbances. Whether or not alterations in function of the parasympathetic center in the hypothalamus are the cause of focal vascular disturbances in the stomach and elsewhere is an important question. One may ask whether a chronic ulcer of the stomach may not have its original inception through some disturbance of the vegetative centers. Can an acute gastric ulcer follow as a result of emotional disturbances which are usually expressed through the autonomic nervous system? Will continuous imbalance of the two major divisions of the autonomic nervous system cause gastric ulceration of a chronic nature? The psychoanalytic school has repeatedly called attention to the improvement which follows psychotherapy in patients who have gastrointestinal disorders, including peptic ulcers. We have all long recognized the importance of the autonomic nervous system in the treatment of patients with chronic peptic ulcer.

DR. BURRILL B. CROHN, New York: Drs. Blackford and Williams have helped to classify the statistics of hemorrhage. In past years hemorrhage was spoken of without analysis of age incidence, sex or complicating factors and without differentiating mild from severe hemorrhage. A first severe hemorrhage may arise from carcinoma; if a first hemorrhage is fatal, the chances favor carcinoma. Secondary hemorrhages are more likely to be benign and are usually less severe. I have not yet met a surgeon who in this country has operated in a case of ulcer hemorrhage in the first twenty-four hours of a severe hemorrhage. Finsterer has formulated his surgical approach: he employs infiltration anesthesia of the abdominal wall, the patient being operated on within the first twenty-four hours, but there is no clear concept of what exactly should be

done. In some cases he uses tamponade against the side of the ulcer, in others he ties off the vessels and in still other cases he resects with exclusion of the duodenum. If one is going to undertake a program of operations for hemorrhage within the first twenty-four hours, one should approach the problem with some sort of understanding of its real significance, risks, mortality and curability.

DR. ANDREW B. RIVERS, Rochester, Minn.: The work of Drs. Blackford and Williams regarding the grave threat to life of massive hemorrhages beyond 45 has borne abundant fruit. They have made all of us more cautious in the handling of these patients. The additional attention lavished on older patients with gastric hemorrhages has saved many lives. I will not quibble about their statistics. I do not quite share their apprehension regarding the danger to life of gross gastric hemorrhage in the younger section of the 45 years and older group, but let's assume that in the older group the proportion of fatalities is about 30 per cent; we are called out to see an old fellow who has just had a massive hemorrhage. The authors have shown us that more often the first hemorrhage is likely to be the fatal one. The diagnosis therefore may be unsettled. The patient may be in shock. His condition is critical. How shall one know whether this patient should be subjected to surgical treatment? Drs. Blackford and Williams believe that the more serious the hemorrhage the more necessary it is to operate on this patient promptly. We have been taught that he has something like a 70 per cent chance of survival if not operated on. If we inveigle a surgeon into a laparotomy, a number of the 70 per cent who would survive otherwise will not then be so fortunate. In my experience it has often been impossible to determine the gravity of the patient's condition for the first twenty-four hours following a gastric hemorrhage. The continuation and recurrence of bleeding or the development of other complications has usually decided the outcome. But granted that our impressions regarding the diagnosis and the extreme gravity of the condition are correct, there is always the probability that such a patient will not survive surgical treatment. Theoretically it sounds simple to clamp a spurting vessel and stop it from bleeding, but actually surgical procedures under such conditions are usually complex and difficult. These deliberations are of vital importance. Our responsibility in these matters is a serious duty. All practitioners of medicine must be made to realize the serious threat to life of a massive hemorrhage in an elderly patient, but do we want them to believe that the treatment of choice under these circumstances is to subject their patients to surgery? If I at 60 was to have a gross stomach hemorrhage and was removed some distance from an expert gastric surgeon, I would rather stake my chance of survival on an ice pack, a hypodermic or two, and a couple of transfusions. Drs. Blackford and Williams have done a fine piece of work by teaching the profession that a gastric hemorrhage in an elderly patient is a complication which requires most careful attention. I believe, however, that conscientiously applied nonsurgical means would ordinarily result in fewer fatalities than would the precipitous employment of operative methods.

DR. HYMAN I. GOLDSTEIN, Camden, N. J.: It is of interest to note with regard to the presentation by Boles and Riggs on "Neurogenic Factors" the publications on the "Hypothalamus" by Haymaker and Anderson (*Internat. Clin.*, June 1940, pp. 226 and 253) and Donald Sheehan ("The Hypothalamus and Gastrointestinal Regulation," 1940). Contributions have been made to our knowledge of such relationship by Schiff (1867), Ebstein (1874), Durante (1916), Brown-Séquard (1876), Pomorski (1892), Keppich (1921), Stahnke (1924), Mogilnitzky (1925), Korsts (1828), Cushing (1932) and others. Frerichs produced ulcer of the stomach in a cat after division of the splanchnic nerves and of the celiac axis. Ebstein, by injuries to the brain and cord in animals, produced ulcers on a hemorrhagic base. Articles by Master and Bunts (1934) and Vonderahe (May 1939) are of interest. William Fabricius Hildanus (1560-1634) knew of the relationship of the brain and gastrointestinal disturbances (*Opera Observationum et Curationum, Francofurti, 1646*)! Several questions might well be put to the authors. Why do young infants get ulcer even without hyperacidity? Bird's patient had normal gastric secre-

tion. Why are so many people with hyperacidity free from ulcer? Why do ulcers occur so frequently in the duodenum with an essentially alkaline secretion? Why do ulcers continue to heal, even in the presence of hyperacidity? Why the not uncommon occurrence of ulcer following extensive burns or some surgical (abdominal) operation? Why do ulcers apparently heal spontaneously in women during pregnancy? Since Celsus (20 A. D.), Aëtius Amidenus (502-575 A. D.), Avicenna (908-1036), Laurentius Phrysen (Fries, 1518), Rembert Dodonaeus (1517-1580), Felix Plater (1534-1614), Marcellus Donatus (1586), Schenck (1595), Forestus (1594) and Jacopo Penada (1793) discussed ulcer of the stomach and duodenum, we have had the problem, still unsolved, of the etiology of peptic ulcer. Let us hope as the result of such work as reported today that a solution to this problem will be found.

DR. ANTHONY BASSLER, New York: I want to express my admiration to Drs. Blackford and Williams for their work in helping to elucidate a difficult question. Those who have to do with the hospital service in the city of New York have a real problem in this question. We have about a thousand deaths in New York from hematemesis, and among the hospitals to which I belong we have about eighty in a year. I should like to say that when a patient is brought in in extreme condition our attitude is one of rest and large doses of morphine and watching, and from then if after about six hours we are not satisfied with the clinical condition of the patient, we pass a tube in the stomach and drain it and we can get a better idea whether the bleeding is continuing than by any other method we have tried so far. I know about the high protein method. If right away we come to the idea that there is probably a pyloric obstruction present, for whatever reason, that case should be considered surgical at once, because our experience has been that these patients die if they have a pyloric obstruction; so that when from the twelfth to the forty-eighth hour there is a continuation of bleeding, dripping from the tube, and particularly if it is of a serosanguineous character, we are very prone to consider that case as surgical within the forty-eighth hour and try not to wait until a full four days has passed, because, if these patients are operated on after the full four days after a massive hemorrhage, they almost invariably die.

DR. HORACE W. SOPER, St. Louis: In 1931 I reported my method of treatment of massive hemorrhage from the stomach by the introduction of the Levine duodenal gastric catheter, thoroughly lavaging the stomach, breaking up the clot, leaving the catheter in place, and employing siphonage. Ordinarily one will get some mucus and small blood clots which may be seen in the glass connecting tube which leads to the container on the floor. Bright red blood in the tube indicates arterial hemorrhage, which of course calls for immediate surgical procedure. In my experience the surgeon has always been able to locate the spurter, ligate it and save the patient.

DR. FREDERICK W. MULSOW, Cedar Rapids, Iowa: I have been making similar studies from death certificates and doctors' records in Cedar Rapids in the last eight years, and during that period we have had sixty-five deaths proved due to peptic ulcer. One difference, apparently, from other records is the number of deaths among women. Of the sixty-five deaths, twenty-three were of women. One other factor, as Drs. Blackford and Williams mentioned, is that death is much more common among older persons. Of those over 50 years of age there were forty-two deaths—about two thirds. Among those over 60 years of age, twelve deaths were due to hemorrhage, eight to perforation and five to obstruction, with surgical operation. Young persons, of course, showed a much higher rate of perforation as the cause of death.

DR. RUSSELL S. BOLES, Philadelphia: Dr. Palmer states that it might be well not to assume that our observations on acute ulceration were directly traceable to the sequence of events we described; that perhaps it would be better to think of the ulcers having occurred incidentally. We cannot agree with Dr. Palmer that the ulcers were incidental for a number of reasons. First I would refer him to the original observations of Cushing, who reported a group of cases in which perforation of acute ulcers occurred following operation for brain

tumor. Surely the acute ulcerations and perforations described by Cushing were not merely incidental to his operations. I would refer Dr. Palmer to the original research work of Drs. Klemperer, Penner and Bernheim which they reported last Monday before the American Gastro-Enterological Association. As a result of prolonged administration of epinephrine intraperitoneally they produced acute ulcers of the stomach which obviously were not incidental but the result of the administration of the epinephrine. Ulcers which occur as a result of experimental production of hypoglycemia, which it is known stimulates the hypothalamic centers, cannot be regarded as incidental. The acute ulcers produced by Hoff and Sheehan and others in the rhesus monkey as a result of irritation of the hypothalamic centers would not seem to be incidental. Last year Dr. Necheles reported before the American Gastro-Enterological Association the occurrence of acute ulceration of the stomach following the ligation of certain blood vessels and this would appear to be experimental confirmation again of our observations. Finally, I would refer Dr. Palmer to the investigative work of Nedzel, who by means of experimental pitressin episodes brought about the production of acute hemorrhagic conditions and acute ulceration of the stomach which definitely were not incidental. For these reasons I believe we are justified in assuming that there is a correlation in the pathologic conditions we have reported and that the ulcers we observed were not purely incidental but were dependent for their production on the associated neurogenic conditions. I am going to request permission for Dr. Riggs to answer the one remaining question about the pathologic changes we have described. I should like to emphasize that our conclusions have been based on the study of a large group of cases by an experienced neuropathologist. For the past five years Dr. Riggs has examined sections of the stomach in every case in which the brain has been removed. This constitutes more than 1,500 cases.

DR. HELENA E. RIGGS, Philadelphia: Dr. Palmer's suggestion that the changes we have demonstrated in the viscera in our cases are due to the agonal state rather than to chronic circulatory insufficiency is rather disturbing to a pathologist. Since the time of Virchow the pathologist has considered an increase of interstitial connective tissue associated with loss of parenchymatous elements as characteristic of chronic passive congestion, i. e. chronic circulatory insufficiency. The very nature of such tissue alterations precludes the possibility of their occurrence in the last few hours before death. As for the gastric mucosal lesion, we have stated that this is acute and therefore must be considered as occurring in the agonal period. However, we do not believe that the mucosal lesion alone constitutes a gastric ulcer. On the basis of experimental and gastroscopic studies, and of our own postmortem examinations, we feel that an acute ulcer is the result of persistent or recurrent alterations in circulatory efficiency to focal areas of the entire gastric wall. In the deep layers this results in chronic degenerative changes; in the mucosa—which has greater regenerative powers—in cyclic destruction and regeneration. Eventually, as we have attempted to demonstrate in our slides, the mucosa fails to regenerate and the acute phase of gastric ulceration passes into the chronic stage. Dr. Palmer has also suggested that the presence of acute gastric lesions in cases of primary intracerebral disease is merely incidental or, at most, associated with terminal failure of circulation. It will be seen from our charts, however, that such gastric lesions occur in cases of primary cerebral disease with a frequency which is statistically significant. Further, it is our experience that in such cases clinical symptoms of acute gastric ulcer, such as melena or blood stained vomitus, frequently occur. As to the effect of circulatory insufficiency on the vegetative nervous system, we have been able to demonstrate clinical signs of vegetative stimulation, such as pupillary changes, pulmonary edema and rapid pulse, in many of the cases which at postmortem showed acute gastric ulcers based on circulatory insufficiency.

DR. JOHN M. BLACKFORD, Seattle: With regard to the mortality rate of 30 per cent, I would emphasize that this represents in our series approximately the mortality of the more serious hemorrhages. Serious hemorrhage was noted in approx-

imately half of all who bled in the older group. I think this is very important because when mortality rates are quoted as only 9, 10 and 15 per cent they are based on hospital admissions with gross hemorrhage at all ages, and that is not the basis of our report of a 30 per cent mortality rate. Dr. Allen's work and our own has emphasized that those are critical hemorrhages which present evidence of great loss of blood and shock and all that goes with it. I want to agree with Dr. Rivers, but if I were in a remote part of the world, with no competent surgeon available and I suffered a gastric hemorrhage, I would not be operated on; however it does seem to me that, if this risk of 30 per cent from serious hemorrhage which is agreed on by a number of men besides myself is correct, then probably the surgeon should be able to work out some method of stopping the hemorrhage, because only in that way can these lives be saved.

RECURRENT PEPTIC ULCER

SITUATION OF RECURRENCES AND THE IMPORTANCE OF STUDIES OF PAIN IN THE RECOGNITION OF SUCH RECURRENCES

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Peptic ulcer is among the most frequent of the organic causes of gastronomic unhappiness, and pain is the most consistent among the complaints of patients who have this disease. Not only is the proper evaluation of pain important in the recognition of peptic ulcerative disease, but much regarding the histopathologic condition of such a lesion can be determined by a critical study of the type, situation and reference of the pain present. Although there is a fairly consistent reduplication of characteristics in the symptomatology of peptic ulcer, there is nevertheless considerable variability in the complaints which patients who have this disease will volunteer. This variability seems reasonable when it is considered that, as peptic ulcer invades successive depths of tissue, definite changes in symptomatology may well occur. As neighboring organs are involved and as normal physiologic processes become increasingly disturbed, symptoms might well arise which would substitute for or complicate a syndrome already established by an original, uncomplicated lesion.

PURPOSE OF THE STUDY

Previously, one of us¹ reported a study of pain caused by ulcers situated in different portions of the gastrointestinal tract. In this study the varying states of pathologic development, as ascertained at operation, were correlated with the symptoms of which the patient had complained immediately prior to laparotomy. Thus, by comparing a sufficient number of such accurately allocated lesions with the symptoms they produced, it was believed that a type of serial-section picture could be constructed which might permit correlation between the various changes of the histopathologic life cycle of ulcer and the changing, painful experiences noted by patients who had such a lesion. It was noted that ulcers which penetrated deeply into the tissues produced shifts of the original pain into secondary regions. In such instances much of the symptom complex set in motion by the previously uncomplicated peptic ulcer was lost.

By studying with sufficient thoroughness the exact situation of the pain and the course over which it was projected, as well as the behavior of the symptoms caused by lesions in various situations and at varying depths of tissue, it was believed that certain information might become available by means of which the anatomic and physiologic problems of abdominal pain and its pathways of conduction could be better understood. In this paper we hope to extend this information by means of an examination of the more common localizations of secondary ulceration following various surgical procedures, and by a discussion of the pain they produce.

PATHWAYS AND MECHANICS OF PAIN

There are three important pathways over which painful impulses originating in peptic ulcer can reach the patient's consciousness:

1. The pathway most commonly used for pain produced in uncomplicated peptic ulcers is probably that which involves the visceral splanchnic nerves. The impulses originate in the wall of the gastrointestinal tract, course along sensory bundles in the sheaths of the splanchnic nerves, cross over through the white rami communicantes of the thoracic nerves and pass along the posterior roots of the spinal nerves, thus reaching the posterior horn of the spinal cord. This type of pain has a quality peculiar to itself. It is usually a rather diffuse type of pain, poorly localized, frequently associated with flatulence and usually not very severe, although at times it may be rather acute and colicky. It is dissipated quickly at times, leaving but little residual soreness and tenderness. Seldom is rigidity of the abdominal muscles associated with such pain, and cutaneous hyperalgesia is usually absent. To explain the genesis of pain arising from viscera which ordinarily seem practically insensitive to the stimuli which produce pain on the surface of the body, the presence of an "adequate stimulus" must be postulated. This "adequate stimulus" has been assumed to be an increase in pressure within the gastrointestinal segments which results in stretching of the circulatory fibers of the viscus. We have reason to believe that this mechanism is not so much one of stretching but rather one of "contracting resistance" of the hardy muscular fibers, as marked distention of circular organs which have lost their muscular contractility frequently produced no splanchnic type of pain. It has been suggested that in the stomach this spasm can be the result of hyperacidity, which acts as a trigger mechanism for the production of such spasm. The ordinary uncomplicated syndrome of peptic ulcer with its recurring painful phenomena, dissipated by food and soda, is probably illustrative of this type of pain-producing mechanism, interpreted along the splanchnic pathway.

2. The varying shifts of pain into secondary regions that occur when the ulcer in its progression begins to venture beyond the confines of the bowel can probably be explained more satisfactorily on the assumption of the existence of a second pathway which supplements the originally utilized splanchnic routes. Painful impulses, it will be remembered, may also be conducted from tissues surrounding the wall of the bowel to the spinal cord over the sensitive cerebrospinal nerves, twigs of which supply the parietal peritoneum and mesentery. This route is designated as the spinal-sensory-somatic pathway.

The shifting type of distress caused by a perforating ulcer is a "referred pain." When the ulcer, because of

From the Division of Medicine, the Mayo Clinic.
1. Rivers, A. B.: Pain in Benign Ulcers of the Esophagus, Stomach and Small Intestine, *J. A. M. A.* 104: 169-174 (Jan. 19) 1935.

its progression, makes contact with tissues supplied by spinal-sensory nerves, pain may be interpreted as being felt along the peripheral cutaneous, more highly differentiating, branches of these same nerves, such as the intercostal nerves.

In a series of ulcers studied by one of us¹ it was found that duodenal ulcers with perforating characteristics produced a shift of pain from the original region to the right upper quadrant of the abdomen and right side of the back. Gastric ulcers so complicated produced a shift of pain toward the left upper abdominal quadrant and the left portions of the thorax and back, whereas perforating gastrojejunal ulcers almost always produced definite shifts of pain downward or through to the back. Such shifts of pain all conform fairly well to peripheral regions supplied by somatic branches that could be expected to be invaded by penetration of such lesions.

3. There seems little doubt at the present time that painful impulses originating in the cardiac portion of the stomach may reach the spinal cord over the phrenic nerves. This pathway is probably utilized rarely, except by perforating lesions invading the diaphragm. One of the most conclusive indications of this pathway is demonstrable in the following report:

A man aged 26 entered the Mayo Clinic complaining of indigestion and pain in the tip of the left shoulder which extended into the base of the neck. This pain arose several hours after meals, and was relieved by eating. Ten years previously gastro-enterostomy had been performed elsewhere because of perforating gastric ulcer. Roentgenograms revealed a deformity high in the stomach. At operation the patient was found to have what appeared to be a perforating gastric ulcer, which had

The phrenic nerve arises mainly from the fourth cervical segment, and to some extent from the third and fifth cervical segments, of the spinal cord. After passing through the thorax it supplies motor fibers to the diaphragm and also supplies sensory fibers to the

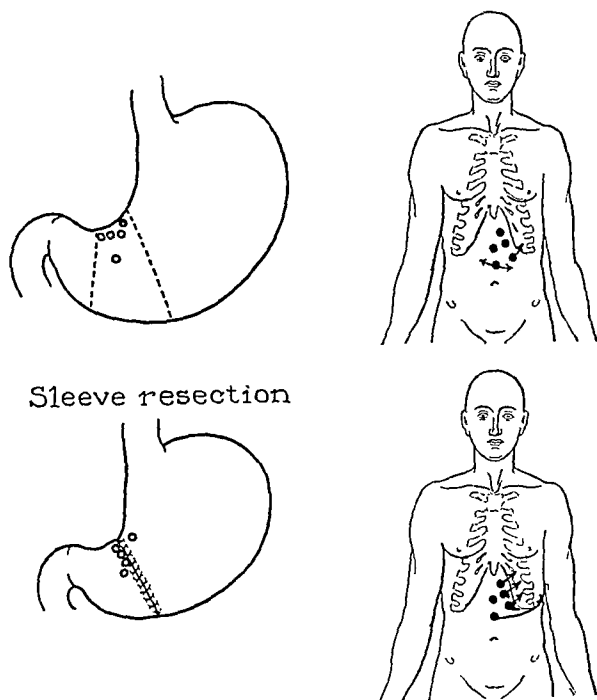


Fig. 2.—Situation of ulcers and direction of the shifts in pain therefrom following sleeve resection.

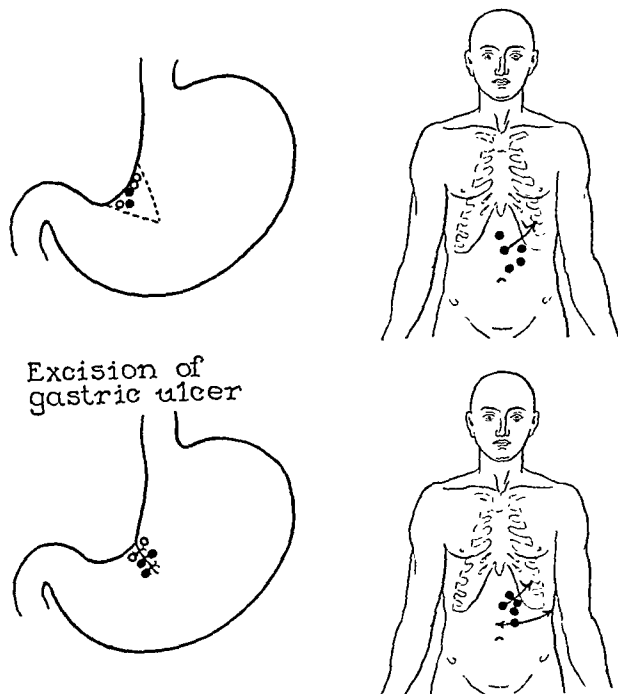


Fig. 1.—Situation of ulcers and direction of the shift in pain therefrom in the case of simple excision.

become adherent to the diaphragm and spleen. Excision of the ulcer was not possible and, as the gastro-enteric stoma was functioning normally, no further surgical procedure was undertaken at that time. The pain in the tip of the shoulder persisted and two weeks following this operation left phrenic emphysema was performed, a procedure which completely relieved the pain in the shoulder and neck.

diaphragmatic pleura as well as to the peritoneum, lining the under surface of the diaphragm. Originating in the same segments of the cord as the phrenic nerve are the suprascapular, supraclavicular and supra-acromial nerves, which are involved in the production of pain in the tip of the shoulder. These nerves may thus be regarded morphologically as the superficial cutaneous branches of the phrenic nerve.

To explain the mechanism of such referred pain, various theories have been advanced. In discussing this, Mackenzie² has the following to offer: "One very attractive explanation is supplied by Ross's³ theory of an 'irritable focus' in the spinal cord." Applying this theory to pain in the tip of the shoulder, it would be supposed that the painful stimuli passing up the phrenic nerves to the third, fourth and fifth cervical segments of the spinal cord produce an irritable focus in the corresponding portion of the posterior horns of gray matter.

Because of this state of irritation, a lowering of the threshold of the cells of the posterior horn results and the consequence is that the stream of afferent stimuli from the cutaneous nerves entering the same segments, although normally silent and unobserved, now becomes capable of producing pain.

Occasionally, pain in the tip of the shoulder is noted on the right side following perforation of a duodenal

2. Mackenzie, James: Remarks on the Meaning and Mechanism of Visceral Pain as Shown by the Study of Visceral and Other Sympathetic (Autonomic) Reflexes: I. Sympathetic Reflexes, *Brit. M. J.* 1: 1449-1454 (June 23), 1906; III. The Mechanism by Which Visceral Pain is Produced, *ibid.* 1: 1523-1528 (June 30) 1906.

3. Ross, James: On the Segmental Distribution of Sensory Disorders, *Brain* 10: 333-361 (Jan.) 1888.

ulcer, an occurrence which Morley⁴ assumes is the result of contact of the irritating fluid with the sensitive under surface of the right portion of the diaphragm. In perforation of a high lying gastric ulcer, pain, if present, is situated usually on the left side.

MATERIAL FOR STUDY

This study includes sixty-five cases of postoperative recurring ulcerations. The exact situation of both primary and secondary lesions was ascertained by roentgenographic evidence. The situation of the secondary ulcerations was confirmed by direct inspection of the tissues at operation. Only those cases were accepted for study which had a history that included exact information regarding the syndrome under consideration.

An inquiry was made as to the situation, duration and character of the pain, the time of its onset and the mode of relief. A special attempt was made to compare the characteristics of the original lesion with those of the one which developed postoperatively. Ten types of operative procedure are included in this group. Each type is illustrated by an illustration (figs. 1 to 10) in which are placed the situations of the primary and secondary ulcerations, together with the situations and extensions of the pain which they produce. Circles indicate lesions of the anterior gastric or intestinal wall and dots indicate ulcers of the posterior wall. Each dot indicates one case and the situation of maximal distress. The arrows indicate the direction of the shifting pain (fig. 1).

Recurring Gastric Ulcer Following Excision.—Occasionally, during surgical procedures undertaken to cure

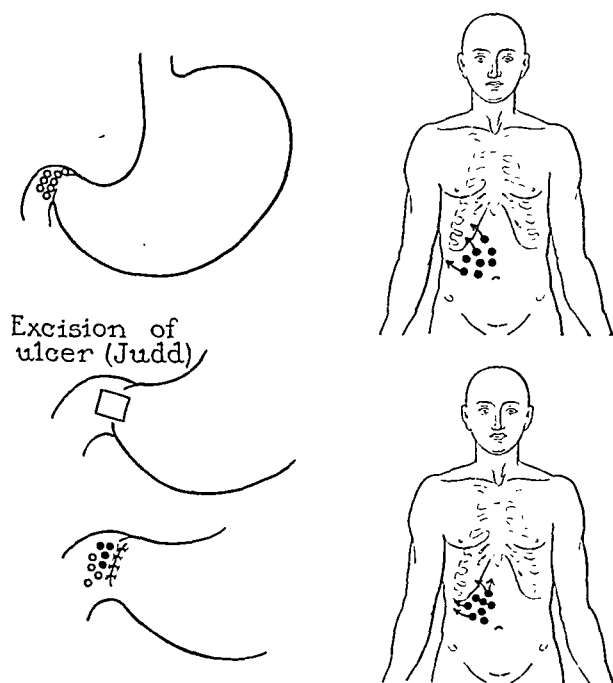


Fig. 3.—Situation of ulcers and direction of the shifts in pain following performance of the Judd type of excision and pyloroplasty.

a gastric ulcer, it is found that the lesion is small and that it will lend itself easily to excision. Unless excision of the ulcer is rather extensive or unless excision with gastro-enterostomy is performed, there is a tendency

for such lesions to recur. If this occurs, the resulting ulceration usually develops in immediate contiguity to, and more often on the pyloric side, of the suture line. The diagnosis of recurring ulcer is usually made without difficulty. Even though there is no distinct roent-

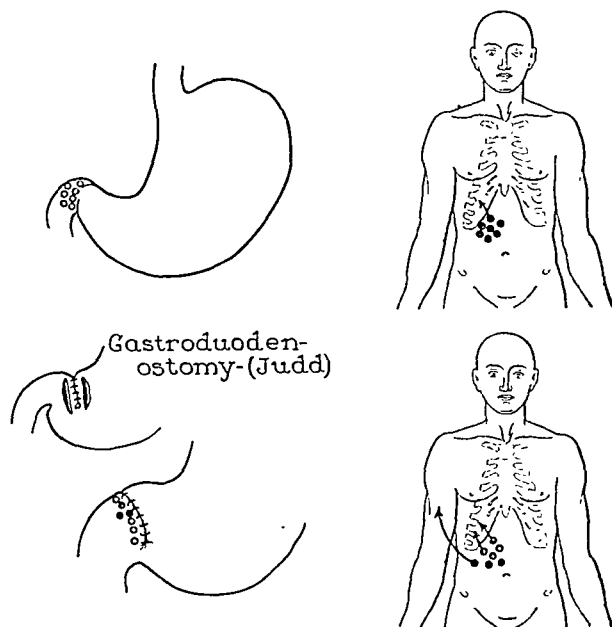


Fig. 4.—Situation of ulcers and direction of the shifts of pain following performance of the Judd type of gastroduodenostomy.

genographic evidence of a lesion, the history of recurring difficulties with pain localized in the region of pre-operative complaint, usually mimicking in almost every detail the original symptoms, is sufficient to make the diagnosis. There is a tendency for these lesions to penetrate, particularly into the pancreas. There is a notorious lack of periodicity in the syndrome of the secondary ulceration, the distress being present almost daily. There is also less tendency to relief by the ingestion of food and alkali (fig. 2).

Recurring Ulcer Following Sleeve Resection.—Several years ago it was not uncommon for surgeons to perform resection of a segment of stomach in which a gastric ulcer was situated and then restore the continuity by end-to-end anastomosis. Other surgical procedures are now employed, and they are so much more successful in dealing with gastric ulcers that sleeve resection is now seldom used. It was found that following the sleeve type of procedure mechanical difficulties developed, resulting in disturbed function of the stomach; furthermore, there was a high incidence of recurring ulceration. Additionally, coexisting duodenal ulcers were not infrequently overlooked during such operations, and consequently, postoperative difficulties were very common. The situation of recurring ulceration following sleeve resection was found to be in or immediately below the suture line. Occasionally, recurrence would take place a short distance above the site of anastomosis. The type of pain caused by primary and secondary ulcers was very similar, although in the latter instance the pain was somewhat more severe than that caused by primary ulcers, with a tendency to shift into the left side of the thorax, a circumstance probably referable to the fact that most of the recurring ulcers were of the perforating type. Again, relief afforded by

⁴ Morley, John: *Abdominal Pain*, Edinburgh, E. and S. Livingstone, 1931.

ingestion of food and soda was not so complete as it had been before the operation for primary ulcers (fig. 3).

Recurring Ulcer Following the Judd Type of Excision and Pyloroplasty.—Judd pointed out that there are certain cases of duodenal ulcer on the anterior wall

was similar to that of the primary lesion. Again, the pain of the recurring lesion proved to be somewhat more constant and intractable than that of the original ulcer. In most instances there was also some mechanical disturbance resulting in a moderate amount of gastric retention.

Recurring Duodenal Ulcer Following the Finney Type of Pyloroplasty.—In figure 5 is illustrated the type of operation devised by Finney for reconstruction of the pyloric outlet, dealing directly with the ulcer and yet achieving adequate anastomosis between the stomach and the duodenum. In some instances this operation was followed by good results and in others by mechanical difficulties; in still another group recurrences of ulcers took place, usually in the vicinity of the anastomosis or slightly below the suture line. Occasionally a second ulcer was found, lower in the duodenum. The situation and symptoms of recurring ulcer following this type of surgical procedure are usually very similar to those experienced at the time of the original ulcer. The region of distress is close to the costal margin, slightly lower than that caused by acute cholecystic disease. Additionally there are the usual signs of organic disturbance and deficiency in gastric emptying, which probably contribute to the inadequacy of relief achieved by the ingestion of food and soda as compared to relief achieved by the same measures directed against the primary lesion.

Recurring Ulcer Following the Billroth I Type of Anastomosis.—This type of Billroth operation has many modifications. However, the principle of these is essentially the same. It consists in removal of the lesion and

in which excision and reconstruction of the pyloric outlet are followed by excellent results. This operation was most commonly employed for young patients who had nonobstructing ulcer in whom there was marked hyperacidity and a small, high lying, hypertonic stomach. The incidence of recurrence, in this group, was rather high. Such recurrences usually developed in the posterior duodenal wall slightly distal to the incision, although occasional recurrences were found in the anterior wall. Unless careful exploration revealed that there was no coexisting ulcer in the posterior duodenal wall, recurring difficulties might rapidly develop from an overlooked lesion on the posterior wall. The symptom complex of these recurring ulcerations was slightly more severe than that caused by the primary lesion. The situation of the pain was similar, with more tendency to extend into the right side of the thorax or back, as is indicated in figure 3. Relief from the pain afforded by ingestion of food and alkali was less marked.

Recurring Ulcer Following Judd Type of Gastro-duodenostomy.—There are certain instances in which anastomosis of the stomach to the uninvolved portion of the duodenum, circumventing the pylorus and the lesion, has been utilized with some success in the treatment of these conditions (fig. 4). The region of the ulcer is avoided and the anastomosis is made entirely in healthy tissue. Although the results of this operation were sometimes good, recurring ulcer not infrequently developed. Such recurrences were found in the duodenum and in many instances were thought to be merely a reactivation of the original ulcer which had failed to heal. The situation of secondary complaints

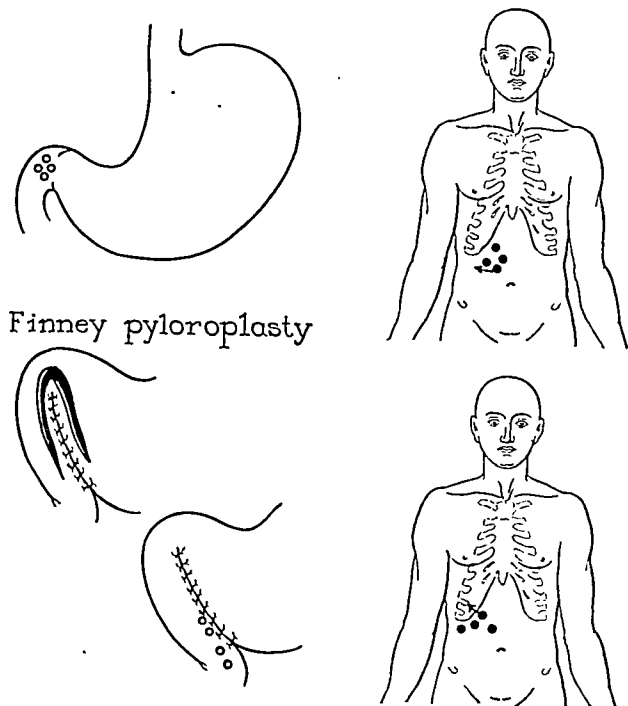


Fig. 5.—Situation of ulcers and direction of the shift in pain following performance of the Finney type of pyloroplasty.

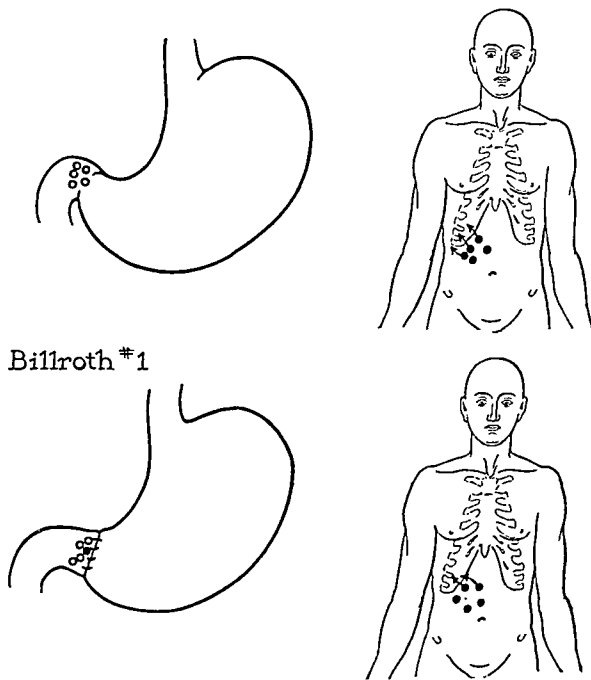


Fig. 6.—Situation of the ulcers and direction of the shifts in pain following performance of the Billroth I type of anastomosis.

the restoration of the gastrointestinal continuity in an end-to-end anastomosis (fig. 6). Some of the patients so treated remained well but recurrences sometimes took place, invariably appearing in the vicinity of the site of anastomosis, usually immediately below the suture line. The marginal ulcer which developed in many of these

patients was often extensive and was complicated not infrequently by hemorrhage or deep penetration. The situation of the original distress was usually definitely to the right of the midline, frequently with reference of pain into the right side of the thorax and back. Recur-

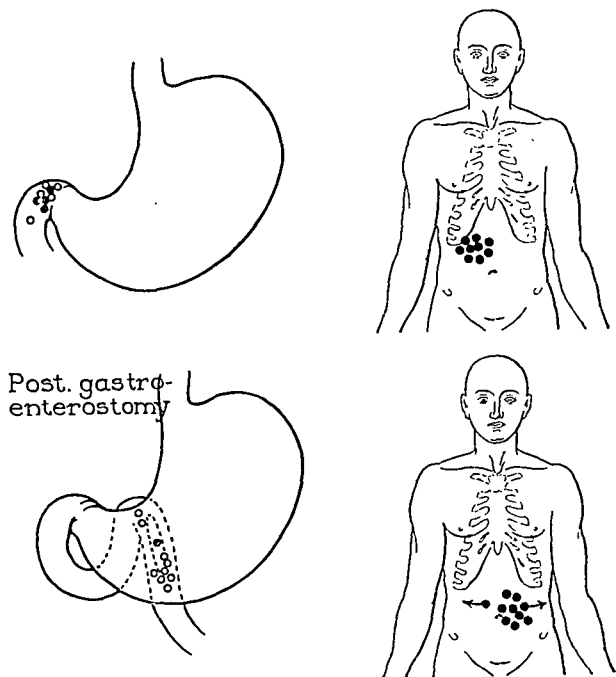


Fig. 7.—Situation of the ulcers and direction of the shifts in pain after posterior gastro-enterostomy for peptic ulcer.

ring ulcers exhibited characteristics almost identical to those for which the operation had been performed. Mechanical difficulties seldom occurred.

Stomal Ulcers Following Posterior Gastro-Enterostomy.—Posterior gastro-enterostomy still remains the operation of choice in many instances of peptic ulcer. A stoma which is properly placed and which is of proper dimensions aids in the adequate emptying of the stomach (fig. 7). The chemical response within the stomach is usually favorable, so that recurring ulceration rarely takes place. Occasionally, however, this type of operation is followed by results which are not entirely satisfactory. The original ulcer in the duodenum may fail to heal, in which instance there is a recurrence of the original symptoms. The distress is then localized above the umbilicus and to the right of the midline.

In figure 7 we have indicated the situation in which secondary ulcerations occur. Most frequently the ulcer is found just distal to the site of anastomosis, often invading the stoma. Next in frequency are ulcers which are definitely jejunal and are found distal to, or opposite, the site of anastomosis. Rarely does the ulcer develop in the proximal loop just above the gastro-enteric stoma. The symptoms of stomal ulcer are similar to those caused by duodenal or gastric ulcer. In most instances these ulcers are of the penetrating type, and consequently there is less periodicity and less tendency toward remission of symptoms. The pain which develops is poorly defined and poorly localized and often is associated with a sense of intestinal unrest which occurs an hour after the meal. Prior to the

development of the pain there is frequently evidence of transitory retention, during which there is loss of appetite, nausea and a vague sense of hypogastric fullness. The situation of pain in uncomplicated gastro-jejunal ulcer is usually to the left and slightly above the umbilicus. If penetration takes place, involving the mesenteric side of the organ, there is almost invariably a shift of pain downward to the left and toward the left iliac region. Less frequently it is found in the right iliac or lumbar regions. Occasionally the pain extends into the scrotal region. Extension to the back of pain caused by penetrating jejunal ulcer is usually definitely lower than that experienced with the original lesion.

Stomal Ulcers Following the Devine Type of Antral Exclusion Operation.—This operation is based on the presumption that the most certain indirect means of obtaining a cure of duodenal ulcer is by excluding it from the irritation of all food and gastric secretion. This type of surgical procedure is illustrated in figure 8. In some instances, however, difficulties arose, as not all the acid-bearing portion of the stomach was excluded by the operation and the duodenal ulcer failed to heal. More often recurring difficulties resulted from the development of stomal ulcers involving the anastomosis or approximating it on either the gastric or the jejunal side. The symptomatology of recurring ulceration had characteristics simulating those for which the operation had been performed, although the situation of the distress was usually farther to the left than that caused by the original lesion. A majority of the recurrences were perforating in type, and in these, especially when

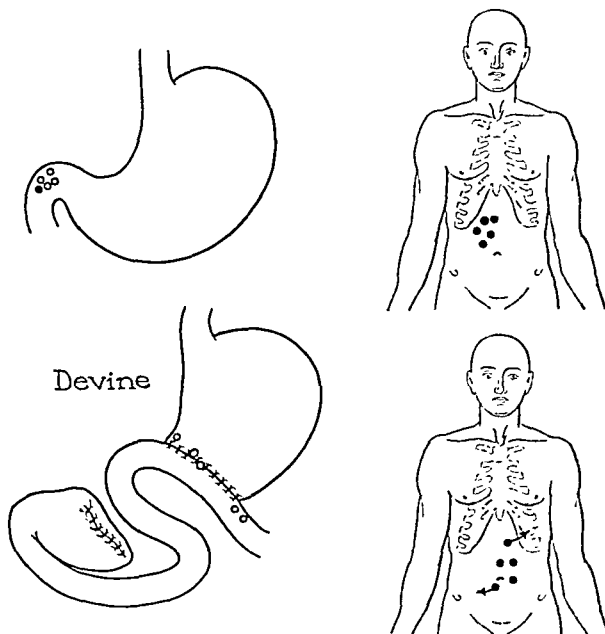


Fig. 8.—Situation of ulcers and direction of the shifts in pain after the Devine type of antral exclusion operation.

they were jejunal in situation, there was a shift of pain into the left iliac region.

Stomal Ulcers Following the Billroth II Type of Anastomosis.—The principle of this Billroth II anastomosis is similar to that of the Devine operation, but a posterior side-to-side anastomosis is made. Occasionally, following this type of surgical treatment, ulcer

developed around the gastro-enteric stoma, as is indicated in figure 9. In one instance an ulcer recurring after this type of operation was gastric in situation. This ulcer may have been overlooked at the time of the operation. In some cases ulceration may have taken

and is somewhat relieved by food or soda. This may be caused by shallow gastric ulcers accompanying a post-operative gastritis.

COMMENT

In evaluating the complaints of the patient who has been operated on previously for peptic ulcer in order to treat such a patient for recurrent ulcers, it is important for the physician to have accurate information regarding the type of surgical procedure which was performed. It is also advantageous for him to be acquainted with the details of the preoperative complaints. A duodenal deformity does not imply that an active duodenal ulcer is present and the persistence of symptoms following operation which were not caused by ulcer would be the rule rather than the exception in such a circumstance. If, on the other hand, symptoms obviously referable to ulcer persist following an operation, it is safe to assume that the original ulcer is not healing or that a second ulcer was present at operation and was not discovered. If scrutiny of preoperative complaints reveals the fact that there was localized distress in two definitely separated regions, for instance, one to the right and slightly above the umbilicus and the other approximating the left costal margin, and if surgical attention had been directed toward only one lesion, persisting symptoms in one of these regions are almost certain to indicate an overlooked ulcer. Persistence of distress in the upper right abdominal quadrant, with characteristics of ulcer following an operation during which an anterior duodenal ulcer had been excised or pyloroplasty performed, indicates with accuracy that a second ulcer, probably on the posterior duodenal wall, was not discovered by the surgeon. If, following an operation performed for an active peptic

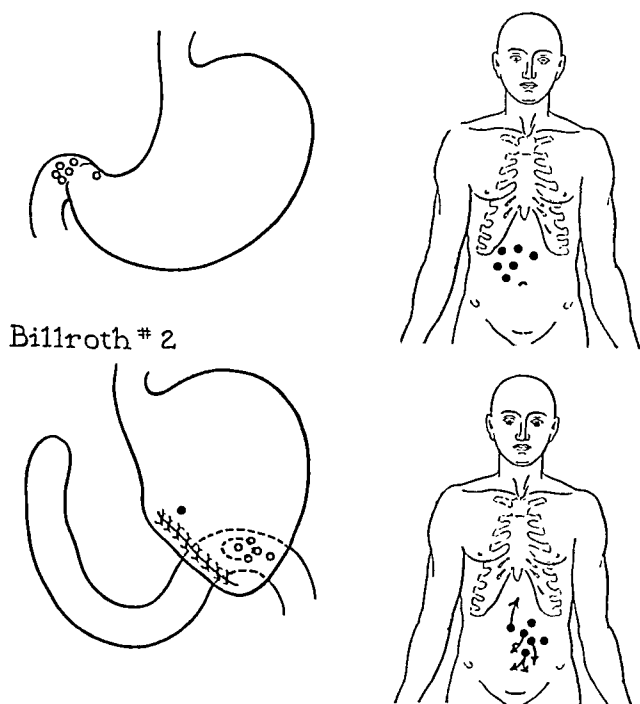


Fig. 9.—Situation of the ulcers and direction of the shifts in pain after performance of the Billroth II type of anastomosis.

place in the jejunal or immediately above the gastro-intestinal stoma. Situation of the pain of these recurring lesions was usually to the left of that caused by the original ulcer and was usually above the umbilicus, when the ulcer involved both gastric and jejunal segments. When the ulcer was found to have involved jejunal segments alone, the pain was usually indicated as being at the level of, or below, the umbilicus. Again, the majority of these lesions were of the perforating type and under such circumstances produced a shift of pain downward toward the left iliac region.

Stomal Ulcers Following Resection and Polya Type of Anastomosis.—Although recurring ulceration following partial gastrectomy with a Polya type of anastomosis (fig. 10) is not a common occurrence, nevertheless it does happen sufficiently often that it must be considered in evaluating the symptomatology of patients who present themselves with recurring difficulties following this type of surgical procedure. The patients included in the present study all had duodenal ulcers as the original lesion. Recurring ulcerations such as these usually involve the site of anastomosis or are found near it. Occasionally the recurrence takes place below the site of anastomosis or, rarely, on its gastric side. The pain of which the patients complain is situated to the left and below that caused by the original lesion. In most instances these ulcers perforate more deeply than did the original ulcers, so that the symptoms they produce are more severe and more intractable to measures for obtaining relief than were those of the original lesions. At times a poorly localizable pain persists or develops following other types of operation; it is localized in the left upper abdominal quadrant. This distress reaches its maximum several hours after meals

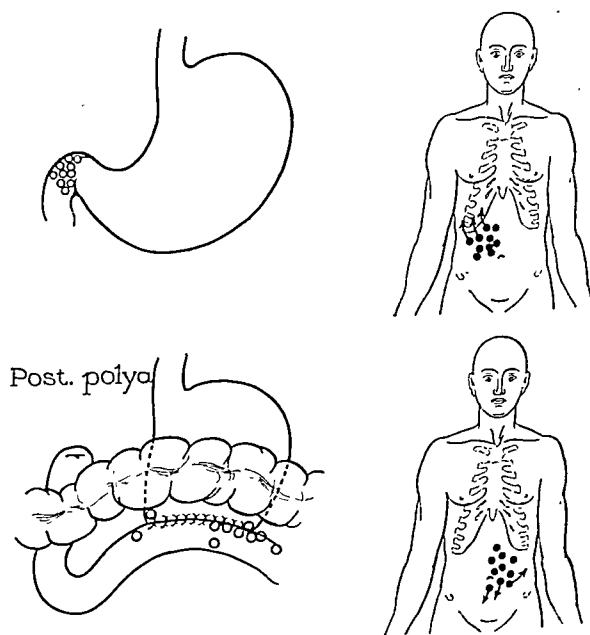


Fig. 10.—Situation of the ulcers and direction of the shifts in pain after performance of resection and a Polya type of anastomosis.

ulcer, the patient enjoys a comfortable period subsequent to which symptoms characteristic of ulcer again result, it remains only to determine where more ulceration has occurred. The situation of the distress and its coincidence with the preoperative region of complaint now becomes important. If the original ulcer was

duodenal and if the region of distress was localized to the right and slightly above the umbilicus, and if the recurring distress conforms in situation to this region, the recurring cause of the complaint is again likely to be duodenal. In the event that the original ulcer was gastric in situation, a recurring ulcer in the same situation would almost invariably cause the reappearance of the complaints which accompanied the original lesion. This is very definitely true if, with the original ulcer, there had been a shifting of pain into secondary regions and if the recurring syndrome included an identical shift of the pain. Roentgenologic investigation remains of paramount importance in the recognition of secondary or recurring ulcers. There are times, however, when accurate and critical studies of situation, type and reference of pain caused by such lesions furnish more accurate information regarding their situation and histopathologic condition than is possible by any other means except direct inspection of tissues.

The closer the recurring ulcer is to the original lesion, the more nearly identical will be the recurring syndrome to the original syndrome. When operations are performed which permanently drain an acid chyme on jejunal mucosa, ulceration occasionally develops in the gastro-enteric stoma or in the jejunal segment contiguous to the new opening. More often this erosion occurs in the path of the draining chyme below the site of the stoma.

If the ulceration occurs at the site of anastomosis, both gastric and jejunal segments may be involved equally, resulting in pain which, although it is situated farther to the left than it would be if the original lesion had been duodenal in situation, is no lower than that experienced by the patient prior to the operation. Should the ulcer, however, develop in the jejunal segment, the situation of the resultant distress usually is in a lower region. When such an ulcer deeply invades tissues, projecting its inflammatory reactions to tissues surrounding the bowel, a secondary shift of pain occurs which is usually definitely lower in situation than the original distress.

The general character of the symptoms produced by the secondary ulcer is similar to that of the first. The pain caused by a shallow peptic lesion is usually difficult to localize unless it produces mechanical disturbances, and this is true regardless of the position of such a lesion. It may produce no pain at all.

A majority of secondary ulcerations, however, tend to penetrate the tissues, and when the deeper tissues of a viscus are invaded there is a tendency for the syndrome to become more definite. The region of pain can usually be indicated with fair precision. With the onset of this secondary pain, other changes in the characteristics of the syndrome experienced by these patients frequently develop. There is less tendency toward intermittence of symptoms, less relief from distress by food or alkalis, earlier onset of pain following meals, and more distress at night. Frequently abdominal tenderness becomes noticeable, and a rather persistent sensation of soreness may develop which usually is maximal over the region of pain. Often this pain does not conform to the usual sequence of pain accompanying ulcer. This is particularly noticeable when extensive inflammatory reactions pass beyond the confines of the bowel and invade tissues surrounding the viscus.

As has been indicated previously, penetration of the ulcer causes projection of pain into secondary regions. This is as true for the secondary as for the primary

lesion. The direction of pain projection depends on the situation of the secondary lesion. Thus, if the lesion is in the duodenum, it is projected into the region of the liver or right side of the back. In gastric lesions the pain is projected upward to the left side of the thorax or back. The pain of jejunal lesions is situated at about the umbilicus or slightly to the left of it and shifts downward into the left lower quadrant of the abdomen or, rarely, into the right lower abdominal quadrant.

In recurring ulceration, especially in lesions involving the stoma, more or less obstruction develops and produces distortion of the usual syndrome of ulcer. The "pain-food-ease" sequence is often lacking and the retention type of vomiting may develop. In the presence of such a complication the distress is usually indicated as diffusely spread out over the epigastrium. This is so regardless of the position of the lesion causing the obstruction.

The results of the present study of secondary ulceration tend to confirm such impressions as those which one of us (Rivers) previously expressed concerning the mechanism of the conduction of pain from peptic ulcerative lesions to the spinal cord. Uncomplicated peptic ulcer probably indicates its presence as a visceral phenomenon which asserts itself along the splanchnic nerves. Such a route, however, does not satisfactorily explain the varying shifts of pain that occur when ulcers venture beyond the confines of the bowel. These shifts of pain probably can be explained better by reference to one of the other mechanisms which we have previously discussed. Such mechanisms would include either the phrenic pathway in the case of high-lying perforating gastric lesion or a route along the sensory spinal nerves. Those nerves could be expected to produce a syndrome less rhythmic and clearcut than the syndrome caused by uncomplicated ulcer, since they are sensitive to many stimuli in addition to the "adequate stimulus" producing pain over the splanchnic route.

CONCLUSIONS

1. The situation of the majority of recurring peptic ulcerations is in or near the site of surgical anastomosis if operation has been performed. The physical factor probably determines the site at which the ulcer will develop. The situation of maximal force of impingement of the chyme decides the situation of erosion.

2. The general characteristics of the symptoms of the recurring lesions are similar to those produced by the original lesions.

3. A majority of secondary ulcerations tend to penetrate deeply and, therefore, produce symptoms which are less intermittent, cause more distress at night and are less easily relieved by food and alkali.

4. A great number of recurring lesions involve the site of surgical anastomosis with the production of more or less obstruction, which tends to distort somewhat the usual syndrome for ulcer.

5. Uncomplicated primary or secondary peptic ulcer probably indicates its presence as a visceral phenomenon, which asserts itself along the splanchnic nerves.

6. The projecting pain of perforating peptic ulcers is in all probability the result of direct stimulation of the spinal sensory nerves which produces referred pain in the distribution of the more highly differentiating peripheral or cutaneous branches of these nerves.

7. When a gastric ulcer begins to produce pain in the tip of the shoulder, indicating use of the phrenic pathway, it can be assumed that deep penetration or active perforation has occurred.

THE EFFECT OF MERSALYL (SALYRGAN) ON PLASMA VOLUME

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In association with the diuresis obtained by mercurial diuretics in cases of congestive heart failure, two strikingly curious phenomena are often observed. Shortly after the intravenous injection of 2 cc. of salyrgan in cases responding to it there is promptly an increased excretion of water which reaches its highest point sharply and then recedes with equal suddenness. Occasional cases are encountered in which the onset of diuresis is slow and its duration longer. In general, however, the outstanding feature of the effect of such diuretics is the sharpness of the reaction and its relative shortness of duration. This fact is well demonstrated in chart 1.

Five patients with varying degrees of congestive heart failure were given by vein 2 cc. of salyrgan. They were

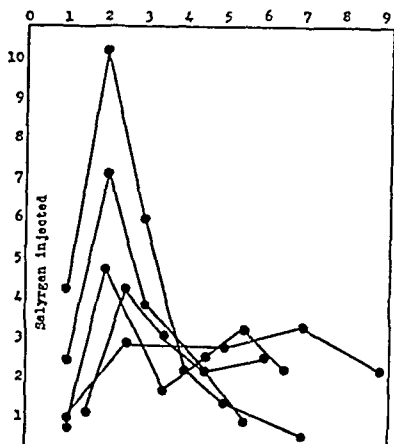


Chart 1.—The diuretic effect of salyrgan, expressed in rate of excretion by urine per minute during a period of several hours after the drug was injected.

asked to empty their bladders at hourly intervals thereafter and the amount of urine excreted in each instance was measured and tabulated on the basis of cubic centimeters of urine excreted per minute during the period of observation. In each instance the severity of the diuresis so induced varied though the general trend of the curve was the same. Along with the increased excretion of

water that may follow the injection of salyrgan there is also a sharp increase in the excretion of sodium chloride and to a less extent of nitrogen. The most striking clinical response to a mercurial diuretic therefore is the rapid excretion of large amounts of water and sodium chloride, which takes place during a relatively short period of time after the drug is injected.

There has been a lengthy debate concerning the precise manner in which these well known responses to the diuretic effect of mercury are brought about. When merbaphen (novasurol) first came into clinical use Saxl and Heilig,¹ Nonnenbruch,² Bohn³ and Crawford and McIntosh⁴ made observations which led them to believe that an important action of the drug was on the extra-

renal tissues and that the diuresis developed secondary to a temporary hydremia. In contrast, this idea was not accepted by Govaerts,⁵ by Christian and Bartram,⁶ by Bryan, Evans, Fulton and Stead,⁷ by Blumgart, Gilligan, Levy and Brown⁸ or by Evans and Gibson.⁹ These several investigators independently have carried out a series of ingenious experiments which were interpreted to show that the diuretic effect of mercury is due primarily to its action on the kidney, any action on the tissues and blood volume, if this exists at all, being accessory and of minor importance.

In 1937 Gibson and Evans¹⁰ described a new method for estimating plasma volume. In brief, this consists in the employment of an azo dye, "Evans blue," with the determination of its concentration in plasma by the spectrophotometer. They claim that this method is accurate, that it avoids many of the errors inherent in dye methods previously in clinical use for the determination of plasma volume and that, on the whole, it can be employed advantageously in the investigation of a variety of clinical problems. Already they and their collaborators have used this method with pertinent results in several studies.

In the fall of 1937 Dr. Gibson was kind enough to teach us the technic of this method in his laboratory at the Peter Bent Brigham Hospital in Boston. Since then at the Robert Dawson Evans Memorial about 300 plasma volume determinations have been made. In each, Gibson's technic as modified by Gibson and Evelyn¹¹ has been followed meticulously. In our hands, just as has been the experience of Gibson and his co-workers, the method has seemed reliable and has appeared to yield consistent results in different clinical states in which changes in blood volume appear to play a significant part.

It occurred to us that it would be interesting once more to investigate the effect of a mercurial diuretic like salyrgan on blood volume by the means of so accurate a clinical method for estimating blood volume as Gibson's method appears to offer. With this idea in mind seven cases have been studied, certain of them being studied repeatedly. The group included four cases with edema primarily of cardiac rather than renal origin, one case with more nearly renal edema, one normal individual, and one patient recovering from secondary anemia. The general plan of work was as follows:

Early in the morning of the experimental day the patient to be observed was treated in the following manner: A blood sample was withdrawn on which was determined the concentration of albumin and globulin in the plasma and of sodium in the serum. The concentration of chloride, of nonprotein nitrogen and of iron was determined in whole blood, and a red cell count

5. Govaerts, P.: Origine rénale ou tissulaire de la diurèse par und composé mercuriel organique, *Compt. rend. Soc. de biol.* **99**: 647-649 (July 27) 1928.

6. Christian, H. A., and Bartram, E. A.: Experimental Observations on the Action of Diuretics, *Tr. A. Am. Physicians* **47**: 292-303 (May) 1932.

7. Bryan, A. H.; Evans, W. A., Jr.; Fulton, M. N., and Stead, E. A., Jr.: Diuresis Following Administration of Salyrgan: Its Effect on Specific Gravity, the Total Nitrogen and the Colloidal Osmotic Pressure of the Plasma of Normal and of Edematous Dogs, *Arch. Int. Med.* **55**: 735-744 (May) 1935.

8. Blumgart, H. L.; Gilligan, D. R.; Levy, R. C., and Brown, M. G.: The Effect of Diuretics on Water and Salt Metabolism, *Tr. A. Am. Physicians* **47**: 304-307 (May) 1932.

9. Evans, W. A., Jr., and Gibson, J. G., 2d: The Blood Volume in Diuresis, *Am. J. Physiol.* **118**: 251-259 (Feb.) 1937.

10. Gibson, J. G., 2d, and Evans, W. A., Jr.: Clinical Application of a Method Employing the Blue Azo Dye "Evans Blue" and the Spectrophotometer, *J. Clin. Investigation* **16**: 301-316 (May) 1937.

11. Gibson, J. G., 2d, and Evelyn, K. A.: Clinical Studies on the Blood Volume: IV. Adaptation of the Method to the Photoelectric Microcolorimeter, *J. Clin. Investigation* **17**: 153-158 (March) 1938.

From the Robert Dawson Evans Memorial for Clinical Research and Preventive Medicine, Massachusetts Memorial Hospitals.

Read before the Section on Pharmacology and Therapeutics at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Saxl, P., and Heilig, R.: Ueber Die Novasurolidiurese, *Wien. Arch. f. inn. Med.* **3**: 141-152 (Nov.) 1922.

2. Nonnenbruch, W.: Ueber die Wirkung des Novasurols auf Blut und Diurese, *München. med. Wchnschr.* **68**: 1282-1283 (Oct. 7) 1921.

3. Bohn, H.: Fortgesetzte Studien ueber Novasurol, *Deutsches Arch. f. Klin. Med.* **143**: 225-237 (Dec.) 1923.

4. Crawford, J. H., and McIntosh, J. F.: Observations on the Use of Novasurol in Edema Due to Heart Failure, *J. Clin. Investigation* **1**: 333-358 (April) 1925.

was made. A plasma volume determination was then performed and from it and the hematocrit reading was estimated the total blood volume. As soon as the blood necessary for this observation was obtained, 2 cc. of salyrgan was injected by vein. At various intervals up to four hours after the injection of the drug a second series of blood studies was repeated and a second plasma and blood volume determination was made. Other blood samples for chemical studies and blood counts were withdrawn at intervals during the six hour period in which most active diuresis seemed likely to occur. On the following morning a final series of blood chemical studies and a third plasma and blood volume determination was made.

The amount of urine excreted during the interval between the various bleedings was measured, as was the total volume excreted during the twenty hour cycle. The patient was allowed to eat stipulated amounts of food and to drink a measured fluid intake. The patient was weighed at the beginning of the procedure and twenty-four hours later.

The total amount in circulation of the various blood components studied was charted at different time intervals during the period of diuresis on the basis of the plasma and blood volume estimation figures, interpolations for these being made when blood samples were

TABLE 1.—*The Effect of Salyrgan on Plasma Volume*

Number	Time	Plasma, Cc.	Per Cent of Corpuscles	Blood, Cc.
1. Cases with No Significant Changes in Plasma and Blood Volume				
1	Before salyrgan	2,650	35	4,120
	4 hours later	2,600	37	4,130
2	Before salyrgan	2,730	29	3,850
	24 hours later	2,630	27	3,600
3	Before salyrgan	2,550	42	4,400
	2 hours later	2,640	42	4,550
	24 hours later	2,570	43	4,510
2. Cases with First a Gain in Plasma and Blood Volume Followed by Secondary Loss				
1	Before salyrgan	2,870	29	4,040
	3½ hours later	3,060	28	4,250
	24 hours later	2,540	28	3,530
2	Before salyrgan	2,920	33	4,360
	1½ hours later	3,630	32	5,340
	24 hours later	2,630	31	3,510
3. Cases with Loss in Blood and Plasma Volume				
1	Before salyrgan	2,990	50	5,980
	2 hours later	2,750	51	5,390
	24 hours later	2,000	51	5,100
2	Before salyrgan	3,460	45	6,290
	4 hours later	3,260	45	5,930
	24 hours later	3,080	44	5,500
3	Before salyrgan	3,660	42	6,310
	24 hours later	3,020	41	5,120
4. Cases with Gain in Blood and Plasma Volume				
1	Before salyrgan	2,330	28	3,240
	2½ hours later	2,470	29	3,480
	24 hours later	2,760	27	3,780
2	Before salyrgan	3,450	41	5,850
	2 hours later	3,630	42	6,240
3	Before salyrgan	2,420	40	4,030
	24 hours later	2,670	41	4,540

withdrawn at times other than when blood volume determinations were actually made. In this manner we hoped to develop data which would tend to illustrate what happens to the composition of the blood during the period in which an active diuresis from mercury is being induced.

For technical reasons it was impossible in each case to make in perfect detail each of the observations out-

lined. The trend of our results, however, with illustrative data is reported.

Our results in relation to the plasma and blood volume following an injection of salyrgan varied, as may be seen by table 1.

TABLE 2.—*The Effect of Salyrgan on Venous Pressure, Vital Capacity and Circulation Time*

Name	Diagnosis	Date	Venous Pressure, Mm. Water	Vital Capacity, Cc.	Circulation Time, Sec.	Time
T	Normal.....	May 18	85	3,800	11.5	Before salyrgan
			—	3,750	12	1 hour later
			65	3,800	11	24 hours later
M	Pyelonephritis; cardiac and renal edema	Jan. 24	160	1,100	13	Before salyrgan
			148	1,150	14	3 hours later
			185	1,100	10	24 hours later
		Feb. 9	130	1,700	16	Before salyrgan
			95	1,600	18	4 hours later
			—	1,700	19	24 hours later
P	Congestive failure	June 1	103	1,950	16.5	Before salyrgan
			90	1,500	16	2 hours later
			110	1,500	13	24 hours later
S	Congestive failure	June 13	120	3,100	25	Before salyrgan
			115	2,800	27	1 hour later
			—	3,300	21	24 hours later
W	Congestive failure	June 13	68	1,700	36	Before salyrgan
			45	1,625	36	1 hour later
			80	1,850	25	24 hours later
McM	Secondary anemia	Feb. 24	100	1,400	16	Before salyrgan
			95	1,400	20	6 hours later
N	Congestive failure	April 3	100	3,000	17	Before salyrgan
			—	2,600	14	1½ hours later
		March 13	75	2,950	14	24 hours later
			85	1,150	45	Before salyrgan
			105	1,100	46	3½ hours later
			80	1,400	—	24 hours later
		April 25	105	1,050	30	Before salyrgan
			95	1,200	47	1½ hours later
			105	1,150	44	24 hours later
		May 4	135	1,200	49	Before salyrgan
			180	1,150	49	1½ hours later
			120	1,300	44	24 hours later

There were three instances in which there was no significant change in plasma or blood volume. There were two instances in which there appeared shortly after the injection of the diuretic an initial gain in plasma and blood volume followed later by a significant loss in circulating blood. There were three instances in which, following the injection of the drug, there appeared to develop a steady and significant loss in plasma and blood volume. There were three instances in which there appeared to develop a steady and significant gain in blood and plasma volume. In brief, our results were entirely inconsistent and appeared to follow no readily comprehensible pattern. Nor is our experience unique: other workers with the problem have faced the same quandary. Brown and Rowntree,¹² studying the volume and composition of the blood by the congo red method and the changes incident to diuresis in cases of edema, found, as did we, that during diuresis changes in blood volume may occur in any direction—there may develop an increase or decrease or no change in blood and plasma volume. Fehér,¹³ making volume determinations with trypan red three hours after salyrgan injections, found at the height of the diuresis an increased volume: on the other hand, Goldhammer, Leiner and Scherf,¹⁴ making blood volume

12. Brown, G. E., and Rowntree, L. G.: The Volume and Composition of the Blood and the Changes Incident to Diuresis in Cases of Edema. *Arch. Int. Med.* 35:129-146 (Jan.) 1925.

13. Fehér, S.: Salyrgandiurese und zirkulierende Blutmenge. *Wien. klin. Wchnschr.* 42:964-965 (July 18) 1929.

14. Goldhammer, S.; Leiner, G., and Scherf, D.: Ueber die zirkulierende Blutmenge vor und nach der Quecksilberdiurese. *Klin. Wchnschr.* 14:1109-1112 (Aug. 3) 1935.

determinations twenty-four hours after the injection of a mercurial diuretic and using both the carbon monoxide and trypan red methods, found regularly a loss in blood and plasma volume. And somewhere in between were Borruso and Ceccarelli, who, according to Goldhammer and his colleagues, found shortly after the onset of diuresis a diminished blood and plasma volume followed later by an increased volume.

The explanations given for such contradictory observations have differed widely. From the point of view of common sense the reasoning first put forth by Brown and Rowntree remains as satisfactory as any: during a sudden diuresis evanescent blood volume changes easily may take place as the result of rapid contraction or expansion of blood volume from dilution or concentration of the blood; and variable transitory adjustments in blood volume, in blood solids or fluid factors may be

relative sodium retention in comparison with the loss of chloride. There was an initial fall in plasma albumin followed by a secondary rise in spite of the fall in plasma volume. During the first few hours there was a relative rise in the plasma globulin so that for at least three hours after the drug was injected there was a reversal of the albumin-globulin ratio. Eventually this became corrected. The initial fall in chloride, sodium and globulin occurred before diuresis was established; but at the same time there was a loss of plasma volume which does not suggest an immediate mobilization of fluid into the blood stream. Rather, this isolated observation is in agreement with the view of Schmitz¹⁵ and others, who believe that the primary action of salyrgan is on the kidney with a secondary inflow of fluid from the tissue spaces to prevent excessive dehydration of the plasma.

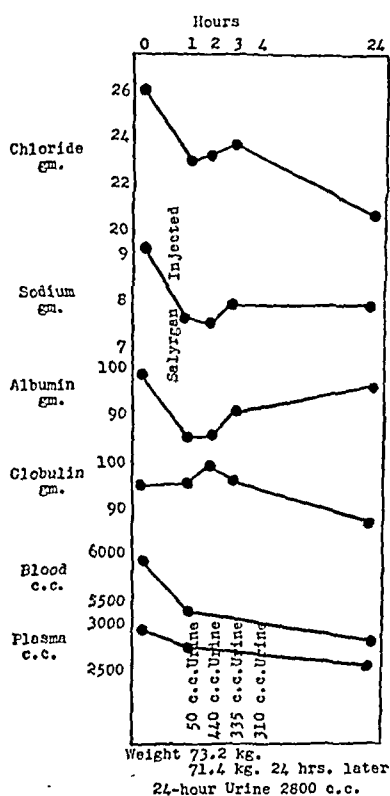


Chart 2.—The effect of salyrgan on blood chemistry.

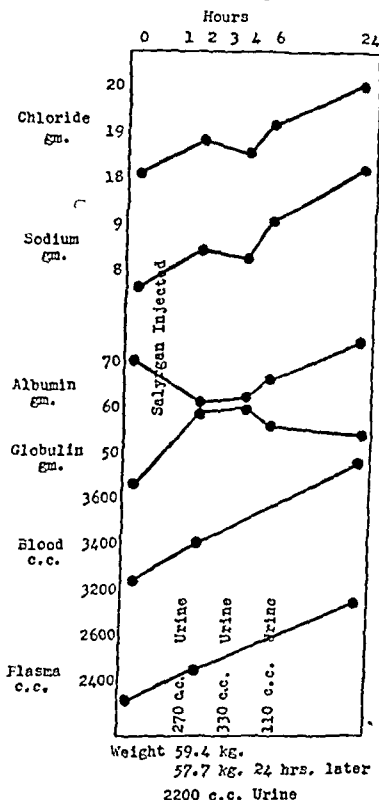


Chart 3.—The effect of salyrgan on blood chemistry.

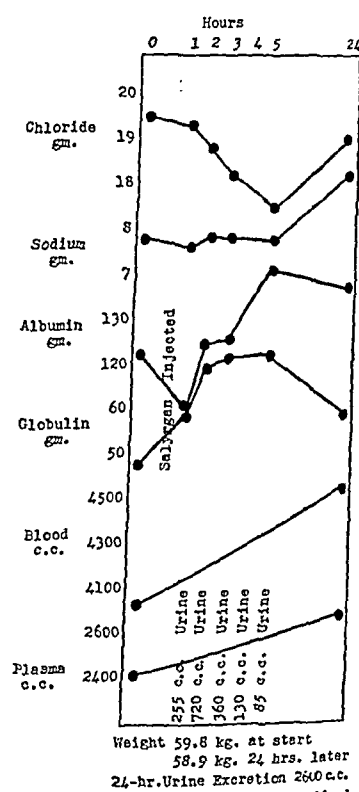


Chart 4.—The effect of salyrgan on blood chemistry.

partially or completely masked by fluctuations in the water content of the blood in the absence of any demonstrable volume changes. One fact remains fairly well established: the injection of salyrgan is likely to be followed fairly promptly by significant changes in the amount of plasma and blood in circulation.

From the chemical data assembled by the methods outlined, the level of blood iron, nonprotein nitrogen and red cells showed only minor and insignificant fluctuations. These figures have been omitted as being unrevealing. The figures in relation to sodium, chloride, albumin and globulin were more noteworthy and are tabulated from three illustrative cases:

The first patient, P., a man in congestive failure, developed a loss in blood and plasma volume following the injection of the diuretic. There developed an immediate fall in blood chloride followed by a slight secondary rise and then a more marked fall as the loss in blood volume continued. There was an initial fall in the serum sodium. But later there appeared to develop a

The second patient, M., a woman with edema from a combination of myocarditis and chronic pyelonephritis, developed an increased blood and plasma volume following the injection of the diuretic. In this instance the diuresis began promptly. There was a steady increase in circulating chloride and sodium and no evidence of any relative sodium retention. There was an initial fall in the circulating albumin followed by a secondary rise: and again a transitory reversal of the albumin-globulin ratio during the period of most active diuresis.

The third patient, McM., a woman recovering from secondary anemia, developed an increase in blood and plasma volume after the diuretic was injected. There was an initial fall in the circulating chloride followed by a secondary rise. There was relative sodium retention. There was an initial fall in the plasma albumin

15. Schmitz, H. L.: Studies on the Action of Diuretics: II. The Effect of Salyrgan on the Water Content of the Plasma as Measured by the Refractive Index, *J. Clin. Investigation* 12: 741-749 (Sept.) 1933.

followed by a secondary rise. There was a transitory reversal of the albumin-globulin ratio during the period of active diuresis, normal relationship becoming reestablished in twenty-four hours. In this case there was an immediate diuresis, reaching its peak during the second hour after the diuretic was injected.

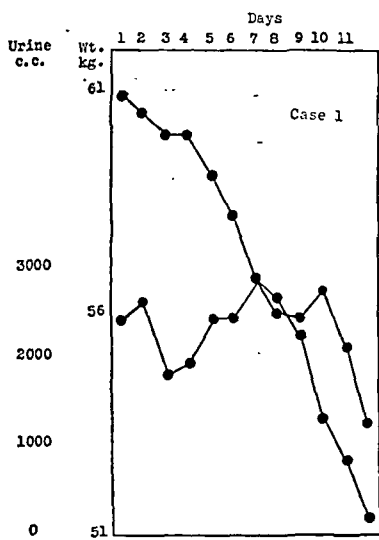


Chart 5.—The effect of mercupurin on urinary output and body weight: In case 1 the drug was injected in three small doses each day. There was a well sustained diuresis and the weight loss followed a fairly straight line.

rationalize by clinical methods the complexities of a diuresis as acute as that produced by salyrgan. But at least they give evidence to show that in connection with the rapid excretion of large amounts of water and sodium chloride after salyrgan there may develop in the blood stream at the same time not only changes in the volume of the circulating blood which are significant but also significant changes in its chemical and physical composition.

Finally our observations bring to light certain practical implications regarding the best use of the mercurial diuretics. Throughout this study the circulation time by the decholin method, the vital capacity and the venous pressure was estimated at the time of each plasma volume determination. The results of these observations are of some interest.

The circulation time after salyrgan in most cases was slightly diminished twenty-four hours after the drug was injected but tended to be slightly prolonged when determined during the time of active diuresis. The vital capacity also tended to be slightly diminished when estimated during the time of active diuresis though increased at the end of the twenty-four hour period. The increases in vital capacity observed in our cases after salyrgan were not as pronounced as in the cases reported by Alsever and Levine;¹⁷ however, the general effect of salyrgan on this particular type of observation was the same in the two series.

The venous pressure in most instances tended to fall after diuresis was established, and usually twenty-four hours later to continue lower than before the diuretic was administered, an observation in agreement with

The behavior of the albumin and globulin in these three cases is worthy of comment, for it is contradictory to Schally's¹⁶ work. This investigator found an increase of the blood albumin after salyrgan injection, explaining his observations on the theory that in order for water to get from the tissue spaces into the capillary circulation albumin must be mobilized as well.

Our experiences, if they do nothing else, emphasize the difficulties entailed in any attempt to

Volini and Levitt's¹⁸ experience. There were exceptions, however, when the immediate effect of the diuretic appeared to be such as to cause temporarily a rise in venous pressure. There was one notable example of this reaction, patient N., on May 4, whose venous pressure rose from 135 mm. of water to 180 mm. a few hours after salyrgan was injected. And for a few bad minutes at the time, the patient was dyspneic and thoroughly uncomfortable. Our blood volume determination at this juncture was imperfect. We suspected, however, that the patient was one of those whose immediate response to salyrgan was an increased blood volume and that such an additional load was more than his circulation could manage comfortably.

Since from our experience it appears unpredictable what may be the immediate effect of a mercurial diuretic such as salyrgan on the blood volume and since striking changes in volume which are potentially harmful may occur quickly, it appears wise to continue with the use of such drugs conservatively and when they are first administered to continue the custom of testing each patient's individual susceptibility to them by the method of graded dosage.

It is possible that salyrgan or other mercurial diuretics may be administered more advantageously in small daily doses over a short period of time than by the single large dose method usually employed when the drug is given at three or four day intervals over a long period. The disadvantage with the traditional way of using a diuretic like salyrgan lies in the intermittence of the diuresis produced. A period of sharp diuresis is

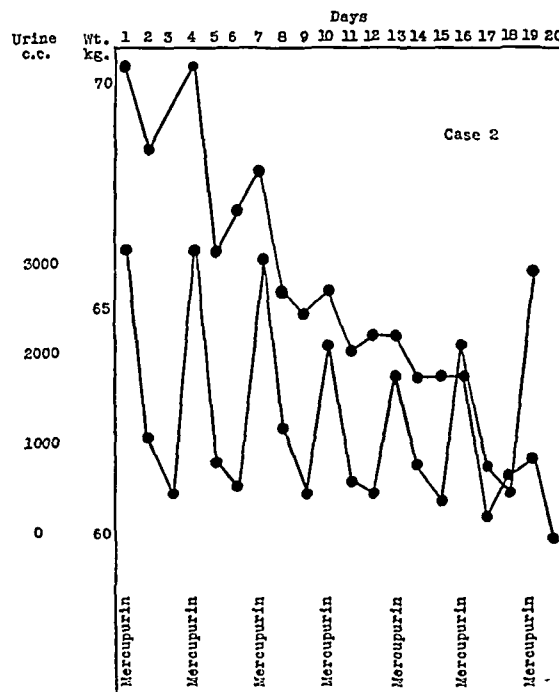


Chart 6.—The effect of mercupurin on urinary output and body weight: In case 2 the drug was injected according to usual precedent in a single dose at three day intervals. The diuresis was intermittent and irregular, as was the loss in weight. The daily fluid intake was constant in both observations. The total amount of drug injected was the same in the two instances.

apt to be followed by a period of relative oliguria and redevelopment of edema. In theory the most effective results from these drugs would be obtained by so grading their dose and its timing that while the drug is in

16. Schally, A. O.: Veränderungen der Bluteiweisskörper bei der Salyrgandiurese, *Deutsches Arch. f. klin. Med.* 177: 368-376 (Dec.) 1934.

17. Alsever, J. B., and Levine, S. A.: The Immediate Effect of Mercurial Diuretics on the Vital Capacity of the Lungs, *Am. Heart J.* 15: 200-205 (Feb.) 1938.

18. Volini, V. F., and Levitt, R. O.: Studies on Mercurial Diuretics: II. The Immediate Effect on the Venous Blood Pressure, *Am. Heart J.* 17: 187-193 (Feb.) 1939.

operation no noteworthy change in the plasma or blood volume develops and at the same time a continuous rather than intermittent diuresis is maintained.

With this idea in mind a few patients in congestive failure and with cardiac edema have been treated over a ten day period with three injections of mercupurin each day, each dose containing 0.5 cc. of the drug. Mercupurin instead of salyrgan was used as a mercurial entirely by chance. The results of these experiments are promising. A steady rather than intermittent diuresis developed and the patients' weight loss also followed a straight rather than a crooked line. The continued use of the diuretic in this manner did no harm: hematuria or other signs of renal irritation did not develop and the concentration of nonprotein nitrogen in the blood did not increase. Subjectively the patients felt notably improved.

CONCLUSION

Studies were undertaken to reinvestigate the effect of salyrgan on plasma and blood volume. The injection of salyrgan may be followed by significant changes in plasma and blood volume which seem inconsistent and which appear to follow no definite pattern. Possibly the sudden increase in blood volume which may occur following the injection of salyrgan is a handicap to a badly diseased heart. Methods of using the mercurial diuretics to avoid abrupt shifts in blood volume and to establish a continued moderate diuresis are possible and seem more logical than to administer such drugs so as to produce a transitory and even uncomfortable diuresis followed by a period of relative oliguria.

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ABSTRACT OF DISCUSSION

DR. LEONARD G. ROWNTREE, Philadelphia: The experiments which have just been reported were broader and more comprehensive in scope than the experiments which Dr. George Brown and I carried on in this connection some fifteen years ago. Dr. Fitz was not satisfied with attempts at measuring plasma and blood volume; he took cognizance of the possibility of dilution phenomena; but even with this added bow to his string it was not possible to arrive at a definite conclusion as to a single mechanism. Apparently there is no one single pattern of change which accompanies the diuresis resulting from this drug. It seems to me that it is within the realm of possibility that the initial state of the blood and plasma may be at least one factor in determining what happens. Dr. Brown and I found, in experiments carried on at that time, that there were great differences in the blood and plasma as we encountered it in different types of edema. For instance, we had edema with low blood volume and low plasma volume and with normal values. We also saw edema with high plasma volume with dilution, and high plasma volume without dilution. These facts may be significant, but I do not believe that they constitute the controlling factor. As a result of all our studies we came to this conclusion, and I would like very much to get the thought of Dr. Swigert and Dr. Fitz on this matter. On the one side there is an edematous body, the kidney, and in between the plasma. One gives this drug and sees the effect, and one comes to the conclusion that the plasma might be just a passive agent and that the effects of the drug are primarily on the tissues or on the kidney, and hence whatever happened to them determined what was happening in the blood volume. The most important part of this contribution is the new method suggested for utilizing these mercurial compounds. I believe that the new method of getting results is infinitely better. It seems that Dr. Swigert and Dr. Fitz started out to do one thing but did not accomplish their purpose very successfully. However, during the process they did something which was more important than what they started out to do. They sought a scientific explanation of diuresis but devised a better method of

treatment, a method which should prove of great value to patients with edema. I should like to ask Dr. Fitz whether he thinks the role of plasma is active or passive. And has he seen any toxic effects from this newer method of employing the drug? Particularly has he seen collapse or hemorrhage attending its use?

DR. MAURICE BRUGER, New York: I should like to discuss the *modus operandi* of mercury diuresis. Although the markedly increased chloride excretion in the urine after the administration of mercury salts is generally appreciated, one frequently fails to realize how pronounced this may be at times. Some eleven years ago, I recall, Dr. Melville and I, while investigating antidotes for mercury bichloride poisoning, injected intravenously 1.2 mg. of mercury bichloride per kilogram into a dog with a bladder fistula. The increased chloride output in the urine was enormous. The control chloride output was 0.013 mg. per minute and within two hours this had increased to 22.4 mg. per minute, representing an increase of some 1,700 per cent. This speaks strongly for the extrarenal factor in mercury diuresis. It was Govaerts, I believe, who by kidney transplant experiments showed that a definite renal factor to account for mercury diuresis also exists. Drs. Swigert and Fitz noted that active salyrgan diuresis frequently placed an extra load on the already impaired heart. Was theophylline ever added to the salyrgan and if so was there any noticeable difference in cardiac efficiency during active diuresis?

DR. GEORGE R. HERRMANN, Galveston, Texas: Our experimental biologist, D. B. Calvin, has been working with this method of blood volume study for the past five years on problems of diuresis in animals. During the past year he has joined G. M. Decherd Jr. and me in a clinical restudy of diuresis mechanisms employing the plasma volume method of Gregerson, Gibson and Stead as modified by Gibson and Evans and by Gibson and Evelyn. In Calvin and Decherd's study in cases of edematous heart failure there weren't so many inconsistencies as Drs. Swigert and Fitz encountered. There were very definite and different trends of plasma shifts following salyrgan and aminophylline and a glucoside from *Digitalis lanata*. We have been interested for a long time in the different mechanisms of the various types of diuretics. In a large series of experiments, some fifteen, with the mercurial salyrgan, there was practically always an early and sustained concentration in the plasma volume that seemed to parallel diuresis. In only two cases were the results discordant. In one case no diuresis followed salyrgan and the plasma volume increased slightly. In the other case a delayed and temporary slight rise in plasma volume was recorded with a subsequent fall as soon as there was an augmentation of the urinary flow. Comparable studies with aminophylline revealed strikingly different plasma volume responses. Immediately after the intravenous aminophylline 0.5 Gm. there was a slight fall followed promptly and uniformly by a conspicuous rise in blood volume, increases considerably greater than those reported by Drs. Swigert and Fitz. This great increase in plasma volume following 0.5 Gm. (7½ grains) of aminophylline intravenously suggested divided dosage as a safety measure. During the time of the most profuse diuresis there was a characteristic tendency in the plasma volume to return toward the initial level. There was a shift in the plasma volume, apparently dependent, in part at least, on the balance established between the tissue fluid mobilization and the urinary output. The end result is usually plasma volume lower than that initially observed. With the glucoside, on the other hand, 2 mg. intravenously for patients with congestive failure, there was a shift in the plasma volume apparently according to the promptness and degree of the myocardial effect of the digitalis preparation. When there was immediate response the plasma volume decreased sharply as a satisfactory urinary output developed. When delayed, the plasma volume remained practically unchanged or increased slightly until diuresis was inaugurated, at which time it decreased.

DR. VERNE W. SWIGERT, Evanston, Ill.: The questions raised in discussion are still unsettled. Further work with regard to the mercurial diuretics and their behavior must be continued.

CHALK GOUT

A REPORT OF TWO CASES WITH A BRIEF SUMMARY OF SOME PREVIOUSLY REPORTED STUDIES ON CALCINOSIS

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The term "chalk gout" is occasionally used to designate a rare disease more generally known as "calcinosis circumscripta." In this condition calcium stones develop in the skin in the vicinity of peripheral joints.

Extensive reviews of the subject of calcinosis have been published during the past two decades: in Germany by Steinitz,¹ in America by Durham² and by Rothstein and Welt,³ in France by Weissenbach and his co-workers⁴ and in England by Atkinson and Weber⁵ and by Brooks.⁶ The first report of this disease in modern medical literature appeared in 1877 (Teissier⁷). However, Holländer⁸ has republished a curious record dated 1654 in which reference is made to a probable instance of this disease.

Steinitz distinguished two clinical types of calcinosis: (1) a circumscribed variety in which the calcium concretions are confined almost exclusively to the regions of the terminal phalanges of the fingers and toes and to the extensor portions of knees and elbows and (2) a diffuse or "universal" calcinosis in which the deposits are widely disseminated. In the diffuse type large portions of the skin may be converted into calcareous plates, or great fluctuant inflammatory masses may appear over which the skin may ulcerate and permit the discharge of gritty, chalk-like material. Interstitial tissues of muscles, tendons and nerve sheaths may be involved in the "universal" types. Internal viscera, however, are spared in both types of calcinosis. In practice, the distinguishing of two types has been applicable only to characteristic instances of the condition. Many individuals have been encountered in whom the pathologic picture was intermediate, fitting neither the circumscribed nor the diffuse type. The condition of these patients has been designated as "transitional." To the present, no constant metabolic or pathologic abnormalities have been found which distinguish either type of chalk gout. Conflicting reports on this phase of the problem have appeared, and the mechanism by

means of which calcium is deposited in both types is uncertain.

In 1938 Atkinson and Weber collected 137 cases of circumscribed calcinosis and seventy-eight of the universal type from the world literature. It appears that information concerning calcinosis must be sought in medical writings by searching under a great variety of names, among which are "tendino-fasciitis calcarea rheumatica," "tendinitis calcarea," "petrificato cutis," "calcinosis interstitialis" or "calcinosis universalis," "Raynaud's disease with calcareous degeneration" and "subcutaneous calcareous granulomata."

Chemically, the chalk stones have been found to consist mainly of calcium phosphate and calcium carbonate. These compounds are generally present in the same proportion as in bone. Small amounts of magnesium carbonate and phosphate, cholesterol and fatty acids have also been found in the deposits.

SPECIAL FEATURES OF CALCINOSIS CIRCUMSCRIPTA

The term "chalk gout" was suggested by Minkowski,⁹ and perhaps independently by Wichmann.⁹ Each, however, used the term "gout" in a different sense. To Minkowski the disease seemed to deserve designation as a form of gout because the deposits near joints of



Fig. 1 (case 1).—The fingers are diffusely enlarged and there is slight flexion contracture at the interphalangeal joints. Over the terminal joints are elevations caused by the underlying chalk stones. The skin over the fingers is tense, firm and shiny and shows scars resulting from the ulceration of previous deposits of calcium.

stonelike calcium concretions resembled the tophaceous deposits of true uratic gout. Wichmann used the term "gout" because he believed that the disease resulted from a special metabolic fault—calcium diathesis analogous to uratic diathesis. Wichmann's contention is not yet proved.

CLINICAL FEATURES OF CALCINOSIS CIRCUMSCRIPTA

Usually this disease runs a mild course. It appears most frequently in elderly persons and somewhat more often in women than in men (in fifty-seven of seventy-one cases collected by Steinitz the patients were females). The disease develops insidiously. Stiffness and aching of joints appear in the affected regions, and the subcutaneous deposits of calcium develop slowly. Calcified regions may or may not be painful. The physician may encounter the deposits by chance in the study of roentgenograms. According to Steinitz, scleroderma or sclerodactylia accompanies calcinosis circumscripta in more than 40 per cent of cases and, as is true in uncomplicated scleroderma, vasospastic phenomena involving the digits occur commonly. These vasospastic symptoms may take the form of characteristic attacks

1. Steinitz, Hermann: *Calcinosis circumscripta ("Kalkgicht") und Calcinosis universalis*, *Ergebn. d. inn. Med. u. Kinderh.* **39**: 216-275, 1931.

2. Durham, R. H.: *Scleroderma and Calcinosis*, *Arch. Int. Med.* **42**: 467-490 (Oct.) 1928.

3. Rothstein, J. L., and Welt, Sara: *Calcinosis Universalis and Calcinosis Circumscripta in Infancy and in Childhood: Three Cases of Calcinosis Universalis, with Review of the Literature*, *Am. J. Dis. Child.* **52**: 368-422 (Aug.) 1936.

4. Weissenbach, R. J.; Basch, Georges, and Basch, Marianne: *Essai critique sur la pathologie des concrétions calcaires des sclérodermies (syndr. de la "Calcinose") et des syndromes voisins*, *Ann. de méd.* **31**: 1-11 (1936).

5. Atkinson, F. R. B., and Weber, F. P.: *Cutaneous and Subcutaneous Calcinosis*, *Brit. J. Dermat.* **50**: 267-310 (June) 1938.

6. Brooks, W. D. W.: *Calcinosis*, *Quart. J. Med.* **27**: 293-319 (July) 1934.

7. Quoted by Steinitz.¹

8. Holländer, Eugen: *Ueber Kalksteingicht*, *Deutsche med. Wchnschr.* **1**: 431-433 (April 5) 1917.

9. Wichmann, Walther: *Ein Fall von Kalkablagerungen unter der Haut (Kalk-Gicht)*, Berlin, E. Ebering, 1910.

similar to those of Raynaud's disease, with the usual series of changes in color involving the acral regions. Some patients complain only of blueness or coldness of the extremities. Ulceration of the skin may occur over the nodules, even in the circumscribed type of the disease, and extrusion of the calcareous material may result.

The Joints.—Descriptions of the status of the joints in patients suffering from calcinosis circumscripta have been very meager in most reports dealing with this disease, although it has been stated commonly that the affected individuals complain of pains in the joints. Costello's¹⁰ patient had "generalized arthritic pains with swelling and thickening of the fingers and toes." Atkinson and Weber stated that the joints are unaffected, meaning that intra-articular disease does not occur. Rothstein and Welt, in their review of calcinosis in children, stated that in one of twenty cases the joints were fixed and motion was limited by the development of contractures. Calcific deposits were found within the joints in two cases. "Chronic arthritis deformans" caused an irregularity and deformity in the articulating surfaces in one case reviewed by these authors. Thus

by the administration of irradiated substances and extracts of parathyroid tissue have not reproduced a syndrome like calcinosis and (4) metabolic studies of calcium in patients who have calcinosis have often yielded normal results, and when abnormal effects have been noted there has been no general agreement concerning, or satisfactory confirmation of, the effects from independent laboratories. Those who favor the hypothesis that local destructive tissue change precedes calcification point to the frequency with which the disease is associated with scleroderma. In scleroderma hyaline changes occur in the subcutaneous tissues. However, in some 60 per cent of cases in Steinitz's series the patients did not have associated scleroderma, and recent histologic studies by Bauer, Marble and Bennett¹¹ have not confirmed the presence of preexisting necrosis of tissue in regions in which calcium has been deposited. The search for an explanation must continue.

REPORT OF CASES

CASE 1.—A woman aged 51 came to the Mayo Clinic complaining of pain and stiffness of the joints. Her medical history was irrelevant excepting that she had never menstruated and had experienced no pregnancies.

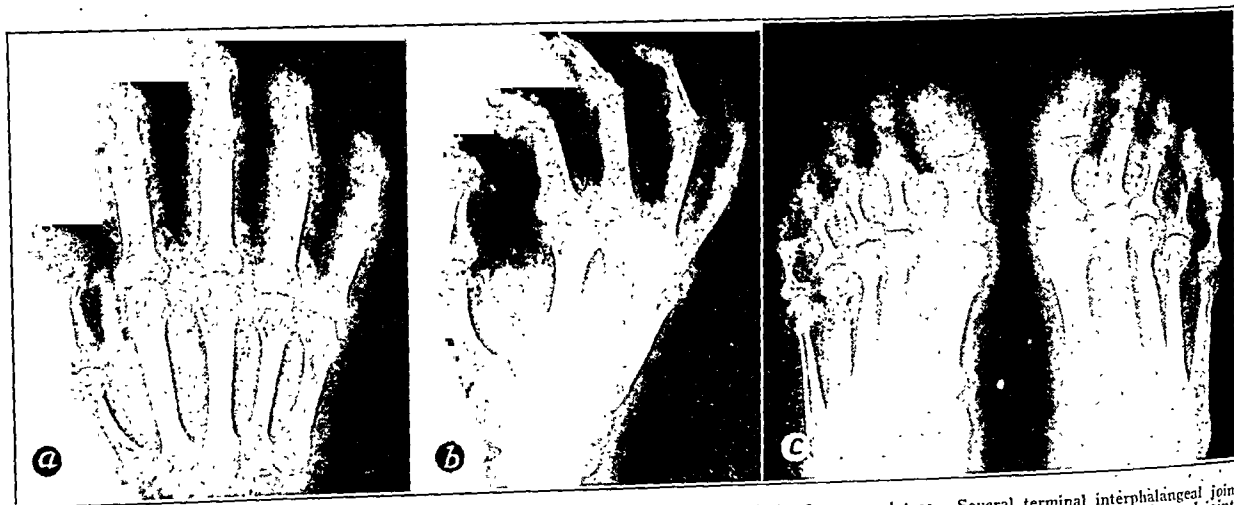


Fig. 2 (case 1).—Deposits of chalk-like material are visible about the phalanges of the fingers and toes. Several terminal interphalangeal joints in the hands have been markedly destroyed by an arthritic process, and similar hypertrophic changes are seen about the midinterphalangeal joints: a, anteroposterior view of right hand; b, lateral view; c, view of feet to show toes.

it would appear that the disease is but rarely associated with the syndrome of progressive chronic atrophic arthritis.

PATHOGENESIS

The mechanism by means of which deposition of calcium develops is unknown. The numerous hypotheses which have been advanced may be divided into two types. The first considers the disease to be a metabolic disorder analogous to uratic gout; the disease is thought to be based on an alteration in calcium chemistry. The second hypothesis holds that the deposition of calcium results after local changes have taken place in connective tissue of such a nature that an increase in affinity for calcium salts exists in the damaged portions. Exponents of both arguments have been unsuccessful thus far in accumulating conclusive evidence. Against the "humoral" theory are the facts that (1) the bony skeleton is usually intact, (2) determinations of the values of various organic and inorganic constituents of the blood have, for the most part, given normal results, (3) experiments in which hypercalcemia was secured

Four years before her visit to the clinic she had noted the gradual onset of dull aching pain in the tips of the toes. Within a few months walking became difficult because of her painful feet. Her knees also became painful. A year after the onset of the disease, the finger tips became painful, especially on attempts to grip, as in turning a doorknob. Within another year, aching and stiffness had extended to elbows and shoulders. The stiffness was particularly marked after inactivity. The patient often attracted considerable attention when she was leaving a theater, because of stiffness and difficulty in straightening to the erect position.

For two years she had noted attacks of pain in the finger tips associated with changes in color from white to bluish red. These occurred when she was exposed to cold. She had obtained relief from these attacks by immersing the hands in warm water.

Results of the physical examination were essentially negative excepting for the extremities. There was limitation of ability to abduct the right shoulder graded 2 (on the basis of 1 to 4). The forearms could be extended only to 175 degrees because of slight contractures in flexion at the elbow joints. There was limitation of motion at the joints of the fingers so that she was unable to close the fists tightly. The fingers were diffusely

10. Costello, M. J.: Cutaneous Calcinosis, New York State J. Med. 35: 1266-1271 (Dec. 15) 1935.

11. Bauer, Walter; Marble, Alexander, and Bennett, G. A.: Further Studies in a Case of Calcification of Subcutaneous Tissue ("Calcinosis Universalis") in a Child, Am. J. M. Sc. 182: 237-251 (Aug.) 1931.

thickened, but no spindle-like enlargement of knuckles was noted. The regions of the terminal phalanges of all the fingers were tender to pressure and the overlying skin was indurated, dry and scaly. On the dorsal aspect of several fingers small subcutaneous nodules could be seen and felt; they were from 2 to 3 mm. in diameter. The skin over some of these nodules appeared to be scarred (fig. 1). In these regions ulceration, discharge of nodules and subsequent healing had occurred. Eight or ten similar nodules could be seen shining through the skin of the lateral aspect of the left elbow, and similar small deposits were present about the anterior aspects of the knees. Both ankles were swollen graded 1+ but were not tender, and the sub-astragaloid regions were markedly limited in range of motion.

Blood counts and examinations of the urine gave essentially negative results. The value for blood calcium was 9.6 mg. per hundred cubic centimeters and for phosphorus 3.4 mg. per hundred cubic centimeters. The value for serum phosphatase was 1.7 units. Roentgenograms of the right hand (fig. 2 a and b) showed extensive destructive changes caused by arthritis, involving the terminal and middle phalangeal joints with heavy deposits of calcium in the subcutaneous tissues of the terminal phalangeal portions and destruction of the adjacent bone of the terminal phalanx. In the roentgenograms of the feet (fig. 2 c) there was

feet, knees and elbows, with dryness and cracking of the skin of the hands. He had been very active in athletics, having participated in football, baseball, track and basketball, thus having been exposed to numerous traumas for many years. The history of the present illness was as follows: Shortly after his enlistment in the army in 1918 he had noticed a stiffness of the hands, with soreness of the joints and a dryness and cracking of the skin of the fingers. To close the hands was painful. He could not play baseball because it caused pain in the hands. Two or three months later he had noticed soreness and stiffness of the joints of the feet and knees. His joints limbered up with exercise. A year which he spent in New Mexico for a change in climate did not help. Alveolectomy and tonsillectomy had been done with no improvement.

During the year before the patient's visit to the clinic, small lumps had appeared in the ends of the fingers, and he said that the tips of the fingers had seemed to feel sore.

He had noted some difficulty in regulation of the temperature in the feet and hands; at times the feet were very cold and could be warmed only with great difficulty, and at times he awakened in the morning with very warm hands, which assumed a normal temperature only after exercise. His hands easily turned blue with chilling.

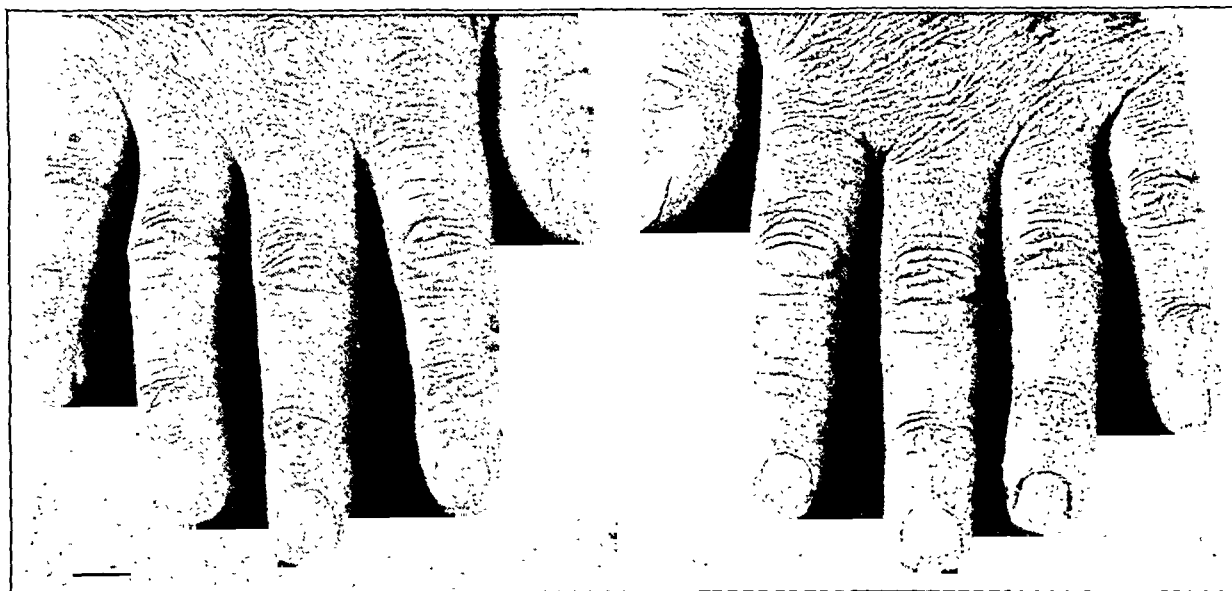


Fig. 3 (case 2).—The skin over the terminal portions of the fingers is cracked, and numerous scars are visible over the region of the terminal interphalangeal joints, where ulceration and discharge of chalk deposits have taken place.

noted marked periostitis of the shafts of the second, third and fourth metatarsal bones bilaterally and evidence of inflammatory and destructive changes in joints involving the tarsal joints. Deposits of calcium were seen about the phalanges of the toes similar to the deposits noted in the hands. A curious portion of subperiosteal rarefaction was noted in the roentgenogram of the left elbow at the site of the two regions of subcutaneous deposition of calcium along the outer aspect of the humerus. Portions of subcutaneous calcification were also noted about the lower aspect of the right knee.

Examination of the capillaries of the nail folds was carried out according to the technic of Lombard.¹² They were very difficult to see because of the deformities of the fingers. However, it was noted that the number of loops was decreased in each field. The individual loops were large, were irregular in shape, and appeared to have marked loss of tone, resembling the capillaries frequently observed in the presence of scleroderma. No results of treatment can be reported at this time.

CASE 2.—A man aged 45 when he came to the Mayo Clinic in 1928 complained chiefly of stiffness and soreness of the hands,

On physical examination the patient was found to be well developed and well nourished. The skin covering the hands was very dry; this was most marked over the dorsal portions of the fingers and especially over the terminal phalangeal joints (fig. 3), where the skin was hard, fissured, shiny and red. The same appearance was noted in the skin overlying the proximal portions of the fingers. The skin over the metacarpophalangeal joints also was dry, shiny and tight. On the end of the thumb and index finger of the right hand and of the thumb, index finger and fourth digit of the left hand, small hard nodules could be felt under the skin. The patient was unable to close his hands completely. The skin over the elbows was dry and somewhat scaly. The skin over the toes was shiny and red but the changes in the skin in this region were less marked than those in the fingers. The skin over the knees was somewhat tight and shiny. Multiple ricelike bodies were noted in the scalp along the upper border of the forehead.

The appearance of the skin was not exactly that presented by scleroderma or Raynaud's disease, although these conditions were simulated by some features of the patient's condition. The cyanosis of the fingers, the trophic changes that have occurred in the skin and the deposits of calcium suggested a vascular disease of the skin.

12. Lombard, W. P.: The Blood Pressure in the Arterioles, Capillaries and Small Veins of the Human Skin, *Am. J. Physiol.* 29: 335-362 (Jan.) 1912.

Routine examination of the urine and the blood counts yielded essentially negative results. The value for serum calcium was 10.2 mg. on one occasion and 9.3 mg. on another determination. Diffusible calcium was 5.0 mg. and nondiffusible calcium was 4.3 mg. The concentration of uric acid in the blood was 3.6 mg. per hundred cubic centimeters.

Roentgenograms of the hands showed slight evidence of hypertrophic arthritis involving the terminal phalangeal joints. Heavy deposits of calcium were seen about the terminal phalanges of the first, second and fourth digits of both hands. The bones did not appear to be diseased on the left side. In the right hand (fig. 4), however, the calcium appeared to have been deposited near regions wherein the bone of the phalanx had been eroded.

PROGNOSIS

Very little information is available regarding the ultimate fate of persons who have this disease. Death has been reported as having been caused by "circulatory weakness," cancer of the stomach, pulmonary tuberculosis, uremia, and asphyxia resulting from obstruction by a bolus of food. Thus the disease in itself is not fatal but death results from intercurrent illness.

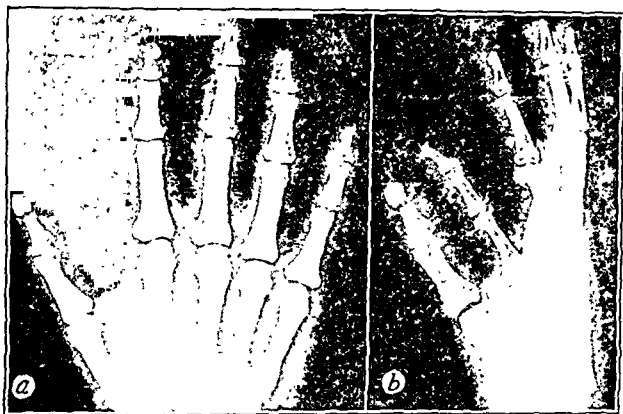


Fig. 4 (case 2).—a, anteroposterior view of right hand; b, lateral view. Heavy deposits of chalk may be seen about the terminal phalangeal regions. The bone has apparently been eroded adjoining some of the deposits. Hypertrophic arthritis (possibly unrelated) may be noted in the terminal interphalangeal joint of the right fifth finger.

TREATMENT

Many treatments have been tried for patients suffering from this disease. Some reputedly have been successful. Surgeons have operated to remove the autonomic nerve supply to blood vessels, to remove the thyroid gland, the parathyroid glands and often to excise the nodules of chalk. Extracts containing the hormones of the pancreas, pituitary body, ovary, parathyroid glands and thyroid glands have been administered. Iodides, phosphates, acetylcholine and other drugs have been tried. Heliotherapy, roentgen therapy, electrophoresis and a lemon diet have been recommended. More recent reports have dealt with interesting attempts to treat this disease by applying newer methods of mobilizing calcium. Craig and Lyall¹³ administered disodium hydrogen phosphate in the attempt to cause interference with the normal absorption of calcium, the expectation being that the bones subsequently would draw on calcium from the deposits of chalk. Kennedy¹⁴ has had success with the use of a ketogenic diet. Ammonium chloride, sodium citrate and parathyroid extract have been used. Some patients have recovered without treatment.

13. Craig, John, and Lyall, Alexander: A Case of Calcinosis Universalis, and Suggested Method of Treatment, *Brit. J. Child. Dis.* 28: 29-34 (Jan.-March) 1931.

14. Kennedy, R. L. J.: Calcinosis and Scleroderma: Treatment of a Case by Use of the Ketogenic Diet, *J. Pediat.* 1: 667-673 (Dec.) 1932.

Clinical Notes, Suggestions and New Instruments

A CASE OF TRICHINOSIS PRESENTING CHEMOSIS OF THE BULBAR CONJUNCTIVA

LOUIS LEHRFELD, M.D., AND CARL F. BREISACHER, M.D.
PHILADELPHIA

Bulbar chemosis, alone or with other symptoms, is not generally considered to be a symptom of trichinosis. Osler¹ considers edema of the eyelids a characteristic symptom but does not call attention to bulbar chemosis in this disease. Foster Moore² makes no mention of it, and it is not described in standard ophthalmologic textbooks.³ There are, however, several references to this symptom in the ophthalmic literature and also in the general medical journals. Parker⁴ in 1907 reported six cases, four of which presented lid and conjunctival edema as the chief complaint. Carter⁵ in 1930 reported three cases and called particular attention to bulbar chemosis as a prominent symptom. Stoll⁶ in 1929 presented two cases in both of which chemosis was the chief complaint. Hickling,⁷ Thomas and Cooper⁸ and Key⁹ have also made mention of this symptom.

REPORT OF CASE

C. F., a white female, first came to the emergency room of the Wills Hospital on April 29, 1940, complaining of swelling of the eyes. She gave a rather indefinite history of slight puffiness of the lids of both eyes with swelling of the "whites of the eyes" beginning about one week prior to admission. The swelling of the lid became less but the swelling of the "white portion" increased, with tearing. A feeling of feverishness and malaise accompanied the ocular symptoms.

On examination, the eyelids of both eyes presented slight swelling, both upper and lower. There was no edema of the face or forehead. The conjunctiva of each eye, particularly the lower bulbar conjunctiva, was intensely chemotic, so marked that it protruded between the lids, preventing complete closure of the latter. The conjunctival vessels were slightly injected and the entire conjunctiva had a yellowish, waxy appearance. Both corners were clear, the irises were normal and the pupils reacted normally. The fundus was normal and healthy bilaterally.

The disease trichinosis was suspected and the patient was referred for a complete blood count the following day. This showed a white cell count of 10,800, of which 53 per cent were neutrophils, 25 per cent eosinophils, 17 per cent small lymphocytes and 5 per cent monocytes. Because of the eosinophilia, the patient was admitted to the Wills Hospital the same day, April 30, for further study.

On admission, the temperature was normal, rose to 99.8 F. the third day, May 2, and continued irregularly thereafter, rising to 105 F. on May 6, thereafter gradually falling. After May 9, until discharge May 17, the fever never rose to above 100 F. and was intermittent. The respiratory rate varied from 18 to 28 a minute, the pulse rate from 88 to 112.

Results of the blood counts are given in the accompanying table.

From the service of Dr. Louis Lehrfeld, Wills Hospital.

1. Osler, William: *Principles and Practice of Medicine*, ed. 11, revised by McCrae, Thomas, New York, D. Appleton & Co., 1931.

2. Moore, R. F.: *Medical Ophthalmology*, ed. 2, London, Churchill Company, 1935.

3. Duke-Elder, W. S.: *Text Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, vol. 2. Berens, Conrad: *The Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936. Fuchs, Ernst: *Diseases of the Eye*, ed. 10 (English), (translated by W. Duane), Philadelphia, J. B. Lippincott Company, 1933.

4. Parker, F. J.: *Eye Symptoms of Trichinosis*, *M. Rec.* 72: 179, 1907.

5. Carter, L. F.: *Trichinosis and Its Ocular Manifestations*, *Tr. Sect. Ophth.*, A. M. A., 1930, pp. 72-82.

6. Stoll, H. F.: *Trichinosis: Two Cases Presenting Diplopia and One, Polyserositis*, *J. A. M. A.* 92: 791-793 (March 9) 1929.

7. Hickling, R. A.: *Edema Around the Eyes Caused by Trichinella Spiralis*, *Brit. M. J.* 2: 654 (Oct. 10) 1931.

8. Thomas, J. B., and Cooper, W.: *Case, Trichinosis with Predominant Symptoms Referable to Eyes and Frontal Sinuses*, *Am. J. Ophth.* 7: 511-512 (July) 1924.

9. Key, B. W.: *Trichinosis: Case with Exophthalmos*, *Tr. Am. Ophth. Soc.* 26: 87-97, 1928.

Laboratory examinations were made; the urine was normal and the Wassermann reaction negative. Dental and rhinologic consultants returned negative reports. The stool was examined but no parasites or ova were found. On May 6 (seven days after admission) a small section of the gastrocnemius muscle was excised, sectioned, stained and examined by Dr. J. H. Clark (Philadelphia General Hospital), who found the encysted larvae of *Trichinella spiralis*.

Dr. C. C. A. Banes, who made a general physical examination, found no signs except the ocular ones already mentioned but concurred in the diagnosis.

Further questioning of the patient produced a dubious history of ingestion of uncooked pork two days before the first symptoms were noted. This was not considered to be the offending material, since the time elapsing between ingestion and the appearance of symptoms was very short.

The clinical course of the disease was extremely mild during hospitalization, there being only mild general malaise in spite of the high fever. The chemosis had disappeared by May 6 (the seventh day after admission), leaving only a slight bulbar injection. No swelling of any other part was noted until three days prior to discharge, when the left ankle was noted to be slightly puffy. This had abated on dismissal from the hospital, May 17.

The only treatment consisted in purging with magnesium sulfate every third day (there was no diarrhea at any time), complete rest in bed and a boric acid flush to the eyes several times daily.

In spite of advice to the contrary, the patient signed her release on May 17 (eighteen days after admission) and when last seen on May 28 was symptom free and apparently in excellent health.

After the patient had been discharged, the sections of gastrocnemius muscle were submitted to Dr. John Bozicevich of the United States Public Health Service for examination.¹⁰ In his opinion the well developed cysts enclosing third stage larvae of *Trichinella spiralis* were indicative of an old infestation, but it was considered that, from the clinical features of the case, there had been a recent superimposed infestation.

Results of Blood Counts

Date	Hemo- globin	Red Blood Cells	White Blood Cells	Neu- tro- phils	Eosino- phils	Baso- phils	Lym- pho- cytes	Mono- cytes
April 29....	82%	4,930,000	10,800	53%	25%	0	17%	5%
May 2.....	82%	4,190,000	10,000	45%	26%	1%	27%	1%
May 3.....	12,800	42%	28%	0	24%	6%
May 9.....	80%	4,030,000	12,300	45%	20%	0	33%	2%
May 14.....	77%	4,430,000	11,500	38%	15%	0	43%	4%
May 17.....	80%	4,500,000	11,800	26%	25%	0	41%	8%

COMMENT

No specific treatment for trichinosis is available. In recent years the use of neosarsphenamine intravenously has been advocated but with varying and questionable results. It was not considered advisable in this case, since it was not one of severe involvement.

The peculiar waxy or yellow jelly-like appearance of the bulbar conjunctiva seen in this case was also observed by Carter.⁵ Herrenschwand¹¹ in 1927 was privileged to study an eye involved by trichinae at autopsy. According to his observations the bulbar conjunctiva showed marked round cell infiltration with a superabundance of goblet cells. Trichinae were present in the ocular muscles, mainly in the belly of the muscle and not near the tendinous attachment. They were present in greater numbers than in the skeletal muscles.

It has been considered that edema of the conjunctiva and lids is concomitant with infestation of the rectus muscles with the trichinae. Verhoeff¹² questions this, however, maintaining that chemosis appears before general muscular symptoms develop.

In most of the cases reported, pain on movement of the eyes was present; but the case here reported did not show this

feature. Also in other cases the edema was more prominent over the insertions of internal and external rectus muscles with small punctate hemorrhages, but this too was absent in our case.

The fact that chemosis is a frequent and prominent symptom of the disease trichinosis has not been adequately stressed. As mentioned previously, Carter⁵ drew attention to this and went so far as to conjecture its presence in 50 per cent of cases. If this is so, it is apparent that many cases are missed by the ophthalmologist. In recent years many writers have reported encysted larvae of *Trichinella spiralis* in muscles of a relatively large percentage of autopsies. In these cases no history of infestation was secured. Perhaps the ophthalmologist can in the future detect more of these cases. The importance of a blood count in any case of conjunctival edema presenting a waxy yellow appearance, and without apparent cause, cannot be overemphasized. Certainly the disease should be kept in mind and not considered remote from the practice of ophthalmology.

Sixteenth and Spring Garden streets.

Special Clinical Article

RECENT DEVELOPMENTS IN THE SUR- GICAL MANAGEMENT OF THE OBSTRUCTING PROSTATE

CLINICAL LECTURE AT NEW YORK SESSION

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NEW YORK

The extraordinary advance of medicine in the surgical specialties is nowhere better illustrated than in the field of prostatic surgery. The past ten years has seen unfolded revolutionary instrumental methods of correction of obstructing prostatism. Naturally this departure from formerly accepted principles has occasioned much discussion, some of which has been constructive. That it has, however, successfully withstood the acid test of time is indicated by the general acceptance on the part of the profession of the method as such after a ten year period of trial and error. Another constructive effect of the many communications on the subject, with their attendant discussions, has been to occasion a reevaluation of the formerly accepted methods of open surgical approach. This state of mind has been and will continue to be the occasion of further progress in technic as well as in other factors. I am well aware of the advanced position assumed by some of my colleagues that instrumental operations have practically replaced open surgery. Since, however, I regard this as a period of evolution, a word of caution is offered against the general acceptance of this point of view.

Psychologic limitations have never been so apparent as in the writings of some of the commentators on the surgery of the prostate gland. Their theses have been in large measure a reflection of personal predilections, aptitude, precepts of their predecessors or environmental influences. If these premises are even in part acceptable, it logically follows that one who presumes to speak or write with even measurable authority should, however he concludes it, begin at least his dissertation in an atmosphere of detachment. The other thought that at once arises which is somewhat removed from the particular subject and perhaps

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10. Bozicevich, John: Personal communication to the authors.
11. Herrenschwand, F.: Eyeball as a Path of Invasion in Human Trichinosis, Arch. f. Ophth. 129: 374-385, 1927.
12. Verhoeff, F. H., in discussion on Carter.⁵

a bit academic but which "sticks out like a sore thumb" is the altogether obvious limitations, professionally speaking, of the young medical man who begins and concludes his institutional medical education under the egis of one educational center.

The romance of the prostate, surgically speaking, is the story of continued progress in technical procedure, improved methods, lowered mortality, briefer hospital domicile, lessened morbidity. When it is realized that these advances vitally affect 25 per cent of male mankind, in other words one fourth of the matured minds and bodies of the male portion of the nation, all concerned in this tremendously constructive piece of sociological endeavor merit the comforting feeling of a job well done. Far from considering the job as finished, however, this situation should be regarded as merely a point of departure to other and greater advances. The complacent will, as always, "miss the boat." With this prelude, let us consider the probable routes of further progression.

One of the great forward steps in suprapubic prostatectomy was the inauguration by Lilienthal of the two step operation. This was a veritable life saving innovation. But "time marches on" and the question arises whether, with the marked progress in technical equipment, there may not be a general reversion to the one step operation. There are two well grounded reasons for interposing this question. First, we have ample clinical experience to justify the belief that the vertical incision for cystotomy, so commonly employed in this country, should, save in exceptional instances, be abandoned. It has nothing to commend it except precedent. It has played a not unimportant role in the high mortality of the past. For the benefit of those who may not have read my prior description, the approach is herewith appended:

A transverse incision 5 cm. in length, 5 cm. above the middle of the symphysis includes the superficial tissues and the muscle sheath. One then separates the muscle longitudinally and the parts are retracted. Prior to incision, the bladder has been filled to two thirds capacity and a catheter is left remaining with loaded syringe attached. At this point the bladder is palpated so that one senses the further expanding organ as the additional fluid is introduced. The operator with sharp dissection then exposes the bladder wall, which is seized with Allis clamps above and below the point where the transverse cut is to be made. It should be emphasized that a transverse incision in the bladder is at once more satisfactory from the standpoint of approach and heals much more kindly than does the vertical. The major steps from this point on apply to either one or two stage removal of the gland. In the two stage, a suitable tube is then introduced through the opening. I employ a fair size mushroom catheter, preferably the angulated type. Then a circular suture is taken and closed snugly about the tube as the mushroom part is brought up against the bladder wall. The sutures are not cut, as they are intended later to be used for traction on the bladder to obliterate spaces for possible infection. The ends of the suture about the tube are then passed through the incised rectus sheath, one above and one below the transverse incision, and when drawn on later and tied, brings the bladder wall close to the abdominal wall. A small piece of rubber dam is introduced and the incision in the sheath closed by No. 3 or 4 chromic gut sutures. Final closure may be made by two or three figure of eight tension sutures.

TREATMENT OF PROSTATIC BED AFTER ENUCLEATION

There has been a gradual change in treatment of this bleeding surface. For many years we remained, as Robert T. Morris facetiously described it, in the era of taxidermy—we stuffed our patients with gauze. Then came the compression bags of Hagner, Pilcher and others; next suture of the cut edges. Later, Harris effected in most of his cases almost complete hemostasis by deep suture. For one or a number of reasons, none of these methods of arrestation have proved so generally acceptable as to rule out the others. It is my hope that the method to be described may prove acceptable, after sufficient trial by others suitably equipped. After suprapubic enucleation of the gland, the cavity is somewhat firmly packed with a long 2 inch gauze roll taken from water at a temperature just about as high as the fingers of the operator can support. Bimanual compression supplements this for a few minutes and the gauze is then removed. Prior to enucleation the patient has been prepared as for a cystoscopy. The visualized electrotome is now introduced through the urethra; suction is begun at the site of the incision as the flow of water through the endoscope is started. One is surprised at the clarity of vision and the precision with which bleeding points can be seen and coagulated with the gap current. Where satisfactory hemostasis is accomplished, the use of packing or the compression bag is unnecessary. When it fails nothing is lost, as the other measures are still available. Finally, it obviates extensive tissue separation should one desire to suture or clamp from above. If the endoscopic method of arrestation of bleeding with the visualized electrotome as here described proves effective on further trial by others as well as by myself, it may obviate the blind and, it may be said, unsurgical method of packing or bag compression in general use today.

My objective in this tentative proposal is to obtain an early decision from a group of qualified workers in this field. Should time and usage prove these technical steps acceptable, it will perhaps be conceded that the important factors which militated against the one stage suprapubic prostatectomy may thus be eliminated. These factors may be summarized as follows: prevesical or perivesical infection; secondary bleeding shortly postoperative, or later bleeding incidental to removal of compression apparatus; discomfort of the patient.

For purpose of clarification my point of view is that infection has been reduced to a minimum by the transverse approach as previously described, the constitutional reaction strikingly lessened and healing hastened. Here the clinical background in the method is sufficient to warrant the assumption that with certain selective exceptions the now generally used vertical incision for suprapubic approach will be abandoned and a reconsideration of the necessity for the two stage operation would appear to be in order.

PERINEAL APPROACH

I have never been completely convinced that most of the technical methods of perineal prostatectomy found in textbooks and monographs have been based on sound anatomic or physiologic principles. With this general assumption, it is in order to particularize. First, the practice of many years of an incision over each of the prominent lateral lobes and the piecemeal removal of such lobes is certainly an error. It is merely a replica of the method of Freyer in suprapubic removal, a method long since abandoned for good and proper reasons. Intra-urethral enucleation is the one rational

method of surgical removal of the prostate, either from above or from below. Thus one conserves the internal sphincter. This may be easily proved by subsequent cystographic study. Then too the impression of the technical difficulties of the operation have been overstressed. The following technic offers a rational and easy method:

The first arm of the incision is transverse, and each terminal of this incision is extended by an additional one downward and outward to the tuberosity of the ischium. These incisions are deepened and the ischio-rectal fossa on each side sufficiently dilated to outline the central tendon. The finger of the left hand is then introduced into the rectum and, with appropriate retraction, the last mentioned structure and the rectourethralis muscle are cut sharply and separated bluntly until the bifurcation of the levator ani muscles is reached. A bougie or a Foley catheter bag on which traction may be exerted, which has previously been passed through the urethra, is now palpated as a guide to its position. From the perineum to this point the anterior wall of the rectum takes a direction upward toward the urethra. It is essential therefore for the occasional operator, and wise for the expert, to give himself the benefit of the palpating finger in the rectum up to this point in the operation. From here on, however, one has to deal in large measure with areolar connective tissue and with a descending anterior rectal wall, which can be separated by blunt dissection up to the fascia of Denonvilliers. Consequently the palpating finger is now withdrawn, new gloves are applied and the dissection is proceeded with as in any surgically clean operation. When the fascia covering the prostate has been incised, also transversely, the prostate is exposed and a transverse incision is made into the prostatic urethra posterior to the verumontanum. The Foley bag is now removed, a firm rubber bag retractor is introduced into the bladder (Parker Sym's type), the prostate brought into the field and the gland removed (intra-urethrally) usually in one piece. From this point on, whatever procedure one elects may be carried out. Only essential details are herein described.

COMMENTARY

I believe (a recently acquired view) that elaborate dissection of the ischio-rectal fossae is unnecessary, that when carried out it prolongs wound healing and adds to the danger of infection. The model of bladder retractor here submitted and which has rested in the archives for many years is a frank copy of the Parker Sym's retractor. In the opinion of those of us who have seen it in operation it is completely satisfactory. As a matter of fact, Parker Sym's, with his three minute prostatectomy of fifteen or twenty years back, had at least some of the essentials of a perfect perineal prostatectomy. He made the usual vertical incision in the perineum such as was used for an external urethrotomy, cut down on a staff in the urethra, introduced his bag and, under traction, enucleated the prostate. The cardinal failure here was his complete indifference to the external sphincter.

The approach described obviates the defects just reviewed. Moreover, in a perineal prostatectomy based on sound anatomic and physiologic consideration there should be no excuse for damage to either sphincters or rectum. The foregoing details on technic are submitted merely as an expression of my present opinion as to the probable lines along which further progress may be achieved. They are presented also as an indi-

cation that I am convinced we are still in a period of evolution; that, unless and until one or another method has definitely established its superiority in average hands, other methods of proved value should not be altogether abandoned. They must be subjected, however, to sustained and critical scrutiny, as the present accepted methods are by no means perfect. Obviously, complacent acceptance has no place in investigative endeavors.

ENDOSCOPIC PROSTATIC RESECTION

The innovation of recent years of endoscopic prostatic resection has successfully withstood an unprecedented avalanche of dogmatic assertion, contentious debate and premature conclusions. Many of the early accidents, the mortalities inherent in a highly technical method, could have been avoided by a more conservative, a more deliberate, approach, a better apprenticeship. The literature is replete with proof of this statement. The late statistics of those with large clinical background reveal gratifying figures on functional result, mortality, morbidity and hospital domicile. In increasing measure throughout the world, the method that I have advocated, with concurrent improvements, is gradually replacing open operations. In some responsible clinics it has practically replaced open surgery. In our clinic, during the early stages of enthusiasm, open surgery was reduced to a minimum; then came a period of resumption of older methods in a moderate percentage. The third era, the present, finds us performing endoscopic resection in an ever growing percentage of our cases.

The technic remains about the same as described in previous communications. Of course, since the advent of the sulfanilamides, we have lost our fear of infection. Operative time is greatly shortened, as the removal of the tissue is done without interruption, to remove the pieces. These are later evacuated by means of an aspiration syringe designed for the purpose. Then too, with more efficient appliances for the after-care and improved cutting and coagulating apparatus, postoperative complications are rare indeed. The one complication that has harassed the method is its appeal to the inexperienced or the audacious. The thing appears simple when performed by the experienced. What the observer fails to note is the necessity for much prior apprenticeship with the panendoscope and an exact knowledge of conformation of these structures in the normal, without which the extent of pathologic departures and factors of safety cannot be correctly interpreted. Adequate and especially trained personnel for postoperative care are equally necessary.

COLLATERAL TOPICS

Transfusion.—This subject is introduced here merely to give expression to a personal point of view. The clotting time, hemoglobin and red cell count, blood grouping and so on should of course be matters of routine, as preoperative preparedness is an important part of the postoperative management. It may be added that a red cell and hemoglobin estimation immediately following operation is also of value. When and if a transfusion is indicated, I believe that fractional transfusion of citrated blood serves the purpose quite as satisfactorily as direct transfusion of whole blood; moreover, it obviates some of the disadvantages of the latter. There is an absence of the psychic manifestations attendant on direct transfusion. It should always be remembered that we frequently are dealing with the arteriosclerotic, the myocarditic type of patient. That when direct transfusion is employed there is a natural

tendency to give larger amounts than with the citrate method, in which small amounts can be administered in the patient's room repeatedly when necessary and the febrile reaction is not so pronounced. It is now some years since I have employed direct transfusion.

Pharmacology.—A very interesting experience was noted with sulfapyridine, in a resection case in which there occurred a secondary bleeding of sufficient importance to send the patient to the cystoscopic room for aspiration of clots and endoscopic coagulation of bleeding points. A hemoglobin and red cell estimation was made at this time, 4,800,000 red cells and 90 per cent hemoglobin. On the same evening one of the interns thought the patient was developing a bronchopneumonia and administered sulfapyridine. Forty-eight hours later, without any additional bleeding, the hemoglobin was 48 per cent, red cells 2,400,000. The drug was immediately discontinued, yet the further drop in hemoglobin and red cell count became so marked as to necessitate fractional transfusion. Caution, therefore, and repeated blood study should be the watchwords with this group. I have, with few exceptions, restricted my patients to small doses of drugs of the sulfonamide group as urinary antiseptics, from 20 to 30 grains (1.3 to 2 Gm.) daily. Generally satisfactory, occasionally it does not work out, when resort is had to more specific study and other methods. Ritter reports a case of bilateral kidney abscess, in one of the public hospitals, wherein the temperature remained low for most of the two months period of intermittent administration of one of the drugs of the group mentioned. At autopsy there were found discrete abscesses of the kidneys together with crystals of the drug in the kidney tissue.

There is also too much empiricism manifested in the matter of administration of proprietary hypnotics, too little scrutiny of or inquiry into the question of possible idiosyncrasies, too little reliance on the pharmacopeia and too much on the drug house man. Paraldehyde in oil, for example, administered by rectal tube in divided doses, while not to be recommended for kissing the baby after administration, is one of the safest and best of all drugs for sedation or as an aid in block anesthesia.

Anesthesia.—Inhalation or general anesthesia is very rarely employed in our work. For brief cystoscopic operative manipulations, intravenous anesthesia is occasionally used. It must be remembered that the margin of safety here is low. One in 100 administrations of a drug customarily employed was followed by a temporary state of coma and the patient was aroused only to fall again into a comatose condition which lasted through three, for us, very anxious days. Fortunately, the condition cleared up without further untoward end result. Inhalation anesthesia in the ordinary urologic operations is merely a labor saving device for the over busy or impatient individual.

Spinal Anesthesia.—This of course is largely a one man job. When it is administered by a variety of interns, things are apt to happen from time to time. For the average prostatic resection or a not too prolonged bladder operation, 50 mg. of one or another of the procaine hydrochloride group will prove both safe and satisfactory when not contraindicated. My technic is to diffuse the drug with the spinal fluid. It has however been noted that when the spinal fluid seems to be under pressure the anesthetic effect is not as prolonged from this amount of drug as under normal conditions. Immediately after the spinal is administered, an intravenous salt solution is begun and the

rate of flow regulated in accordance with the blood pressure readings from the other arm. I am disposed to refrain from the use of morphine or its derivatives in conjunction with the barbiturate group as supplemental to spinal anesthesia because of its depressing effect on the vital centers and the possibility of respiratory failure.

Local Anesthesia.—This is considered here only in conjunction with prostatic resection. Others have reported cases conducted under this type of anesthesia,¹ but its potentiality for good has been ignored. There undoubtedly exists a considerable group of debilitated old men, another small group with antecedent history of anginal attacks, and others wherein one is loath to or refuses to administer inhalation or spinal anesthesia. In many such cases, in my opinion, resection may be successfully done in one or more stages under local anesthesia. It may very well be the practice of the future that the earliest manifestations of prostatic obstruction will be subjected to this simple and safe procedure.

The technic that I employ is as follows: Paraldehyde in oil is administered by rectum in divided doses, beginning some hours prior to operation. With the patient on the operating table a long needle is introduced into the perineum and with the guiding finger in the rectum the needle is passed directly into the prostate in the midline and a 1 per cent solution of procaine hydrochloride is injected. The lateral lobes are then similarly injected. Twenty minutes prior to this step a topical anesthetic solution has been injected into the bladder and urethra. When sufficient time has elapsed, the visualized electrotome is introduced. This instrument is now provided with a new attachment—a long needle with a rack and pinion adjustment affording a back and forth movement. The needle is now introduced into the urethra, first in the midline, and the solution injected under the sphincter as far as the mucosa on its postsphincteric aspect and then well into the lateral lobes on each side. The manipulation is so precise that one can at will and under perfect vision infiltrate any part of the prostatic urethra. While it is to be admitted that I am only in the ground breaking phase of this type of anesthesia in prostatic resection, my experience with it encourages in me the belief in its availability in the type of cases mentioned. I cannot escape the feeling that improper selection of anesthesia in operations on debilitated old men is the major factor in mortality.

Calculous Prostate.—This condition occurs with sufficient frequency to warrant the practice of routine x-ray study. It may also simulate malignancy to the palpating finger. Because of the fact that the ordinary suprapubic or perineal prostatectomy is unsatisfactory in this disease there remain but two methods of attack—total excision of the gland by way of the perineum or endoscopic resection. For a long time I have remained skeptical of the effectiveness of the latter method. Recent experience, however, has been so gratifying that it is my belief the method justifies itself and may enjoy a larger role.

Resection and Malignancy.—Attention has been drawn to the fact that a certain proportion of obstructing prostates, let us say 15 per cent, are actually or potentially malignant. It has also been argued that if such is the case why not employ prostatectomy in all

1. Wishard, W. N., Jr.; Hamer, H. G., and Mertz, H. O.: Local Infiltration Anesthesia of the Prostate Preliminary to Resection, J. A. M. A. 102: 32-35 (Jan. 6) 1934.

such cases by open surgery? This certainly merits full and frank discussion. The first thought that comes to mind is, What has become of the malignant cases in the clinics, wherein the claim is made that only in a considerably smaller percentage of cases has there been any occasion for open surgery? My departmental associates S. E. Kramer and J. S. Ritter have given utterance to some interesting opinions on this question. They report several cases of late carcinomatous manifestations following resection wherein a report of benign hyperplasia was obtained following the usual microscopic examination. I have had one such case. These observers contend that, because of the perhaps more than occasional occurrence of insular prostatic carcinomas in which the usual signs are absent, routine serial study should be made of segregated sections; that the time and expense involved are justified even though but an occasional case of latent malignancy is disclosed when without such scrutinizing study it would not have been so diagnosed. One might also add with a measure of verity that late malignant growths are known to have occurred under similar circumstances following digital enucleation. It should also be remembered that prostatic tissue is not all removed in the usual open prostatectomy. On the credit side of resection it can be said that many patients with relatively early obstruction will submit to resection who would not accept open surgery; that in some at least of these cases, if an orderly painstaking serial study of removed tissue is made, an early malignant growth may be discovered and thereupon subjected to radical surgery. Here is Kramer's and Ritter's recommendation. They advise "that between seventy-five and 150 slides in the larger type of prostate be subjected to careful examination. At the time of operation it is also suggested that the tissue be segregated into five different areas." My counter proposal for purposes of practicality would be three such divisions: the midline area, one lateral lobe and the other lateral lobe. It would seem a reasonable expectation that, under such careful study following every resection, cases of insular or previously overlooked incipient malignant growths would thus come to early positive diagnosis and radical surgery.

Prostatic carcinoma in its earliest stage is a proper subject for radical perineal excision. When, however, they are well defined or extensive, the end result of this type of surgery scarcely justifies the procedure. The problem then is amelioration. Here resection again plays a valuable role. Many such patients may be carried along for a varying period of time in comparative comfort. One such patient comes to mind who, after five years and three resections, still devotes full time to his business pursuits and, to the unsuspecting observer, enjoys seeming good health.

The only supplemental physical agent that I employ in such cases is fractional roentgen therapy, and for several reasons. The pressing one is to obviate late secondary bleeding, a more than occasional observation in malignant conditions. In this connection it has been strikingly effective. Massive doses, however, should be interdicted. The other reason is for the alleviation of pain when present. Here again it is the most durably effective agent. The third is retardation, a term used advisedly as perhaps a bit more accurate than the euphemistic one of arrestation, so frequently enunciated by the proponents of physical therapy in the management of cancer of the genito-urinary tract.

It is evident from the foregoing somewhat sketchy commentary that the prostatic picture of today is far

removed from that of a generation or two past, and those over whose heads hang the portentous shadow of approaching senescence may peer in the nebulous future with considerably less apprehension than could their forbears.

2 East Fifty-Fourth Street.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING CHAPTER, WHICH IS THE SECOND OF A SERIES ON AMPUTATIONS AND ARTIFICIAL LIMBS TO APPEAR IN THIS COLUMN. WHEN COMPLETED, THIS SERIES WILL BE PUBLISHED IN THE FORM OF A HANDBOOK ON AMPUTATIONS. THE COUNCIL WISHES TO EXPRESS ITS APPRECIATION FOR THE COOPERATION OF ITS GROUP OF CONSULTANTS ON ARTIFICIAL LIMBS. THE COUNCIL IS REPRESENTED BY DRS. FRANK D. DICKSON, HARRY E. MOCK, FRANK R. OBER, S. PERRY ROGERS, PAUL STEELE AND PHILIP WILSON, AND THE ASSOCIATION OF LIMB MANUFACTURERS OF AMERICA IS REPRESENTED BY MESSRS. MCCARTHY HANGER SR., W. E. ISLE, JOSEPH A. SPIEVAK, DAVID E. STOLPE AND J. B. KORRADY.

HOWARD A. CARTER, Secretary.

CHAPTER II. GENERAL PRINCIPLES GOVERNING ALL AMPUTATIONS

1. INDICATIONS

There are three general indications for amputations: (1) acute trauma of sufficient severity to prohibit viability of a part of an extremity; (2) disease, including malignant neoplasm, infection which appears incurable locally and which threatens to destroy life, and gangrene due either to diabetes or to local circulatory failure; (3) chronic deformities, congenital or acquired, so disabling that better function can be assured by amputation than by any amount of reconstructive surgery and physical therapy. The type of operation indicated and the degree to which function of the stump may be anticipated are dependent somewhat on the cause for amputation.

A. Trauma.—If a part of an extremity is entirely severed or if it is absolutely apparent that it cannot be saved and restored to useful function, amputation should be performed immediately. Within the first six to twelve hours, during which the wounds may be grossly contaminated but the tissues are not infected, a clean operation can be performed at a site of election with a good chance of primary healing and a good functional stump. After this period of grace has expired the purpose of the amputation usually becomes the saving of life and all viable tissues rather than the creation of a permanent stump, and a secondary amputation is usually indicated when the condition of the limb and the patient permit. This late amputation may be carefully planned and should result in a good stump for functional purposes.

B. Disease.—The saving of life is frequently a paramount consideration in amputations performed for disease. If the surgeon, however, is fully aware of the types of operation most likely to assure a functional stump at the different levels, a good stump can frequently be secured without prejudicing the first consideration in any way.

C. Deformities.—Amputations of useless and seriously disabled extremities are always operations of election. The wishes of the patient can be considered, a thorough study of the possible sites and methods of operation can be made, and the limb-maker can be consulted before the amputation is performed. Every such operation should be clean surgery and every stump created should function well.

2. SURGICAL PRINCIPLES

Certain general surgical principles apply to amputations at any level. The bone must be dealt with in the way best calculated to allow it to withstand pressure without pain. Disarticulation leaves surfaces accustomed to pressure from contiguous bone. In amputations in the continuity of long bones the end is much more likely to withstand pressure if amputation is performed through the cancellous portion near either end than if it is performed through the middle portion where the cortex is thick and the medullary cavity is well defined. Osteoperiosteal procedures such as fusion of the tip of the os calcis to the sawed end of the tibia in the Pirogoff operation and the patella to the cut femur in the Gritti-Stokes operation are very successful if union is obtained, but attempts at similar procedures

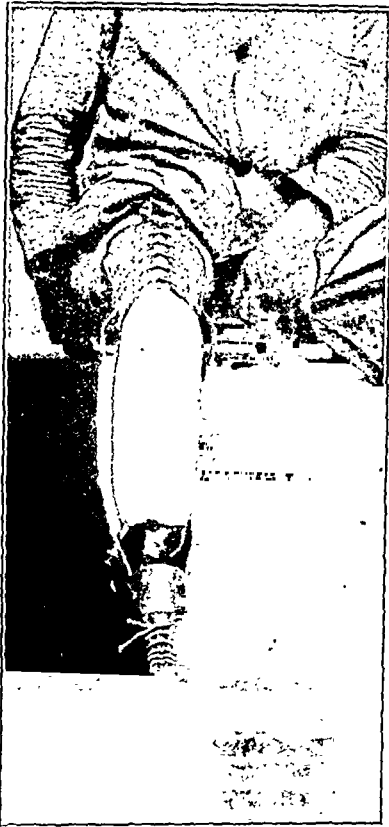


Fig. 1.—Temporary leg with articulated foot and plaster socket for below-knee stump.

in the shaft portions of long bones are not recommended. The tendinoplastic procedures in the lower third of the leg and in the condylar region of the femur are extremely successful in providing painless stumps, capable of sustaining outside pressure. For amputations through the middle portions the "aperiosteal" treatment of the bone is strongly recommended. This consists in removing the periosteum for a distance of from one-half to 1 inch, smoothing off all rough edges from the cortex with a file or rasp and curetting out the medullary cavity for a distance of from one-half to 1 inch.

Proper treatment of the vessels and nerves is imperative. Major arteries must be isolated and carefully ligated. Opinions differ as to the choice between silk and chromic catgut, but with either material a ligature of large caliber and a measure of restraint in drawing it tight will insure against cutting through the vessel wall. Some surgeons prefer double ligations of major arteries. All important nerves should be injected with alcohol of 95 per cent to absolute strength and cut as high as is practicable without exerting strong tension. Careful injection of alcohol into the terminal portion of the nerve makes plastic procedures on the nerve stump unnecessary. Ligation of major nerves distal to the point of injection is advisable.

The problem of the amount and kind of soft tissues with which to cover the bone ends is important. Muscle tissue used for this purpose and subjected to pressure undergoes atrophy and is converted into scar tissue

which is often painful and tender. Broad tendons such as are available behind the lower half of the tibia and in front of the lower fourth of the femur make excellent coverings. Fascia is available everywhere and as covering is second in importance only to skin.

The placement of scars for optimal function of the stump is susceptible to rather definite rules. Plantar flaps provide superior function in amputations of part of the foot and in the osteoplastic and tendinoplastic amputations at the ankle. Anterior flaps are best everywhere between the lower tibia and upper femur. Posterior flaps are preferred when they are available in disarticulation of the hip. In the arm and forearm the end of the stump is subjected to no great amount of pressure, so terminal scars are quite satisfactory. In any situation the bone must be covered with freely movable normal skin with an adequate blood supply and not under tension. For function within a prosthesis, redundancy is as bad as tension. A flabby redundant pad of soft tissues over the end of the bone cannot be fitted well and serves no functional purpose.

3. POSTOPERATIVE CARE

A. *Traction*.—Postoperative skin fixation is advised as a routine procedure. In open amputations skin traction is imperative and should be maintained until healing of the wound is complete. In closed wounds traction is indicated when infection is present or anticipated or when the skin flaps are under considerable tension. Such traction is conveniently applied through wide adhesive straps over a suitable spreader. The many tailed bandage of Scultetus is a convenient and practical outer dressing.

B. *Drainage*.—Surgeons differ on the drainage of amputation wounds. The amount of uncontrolled bleeding and the health of the tissue flaps affect the judgment in each case on this point. If drains are placed, the soft rubber such as is used in making Penrose or cigaret drains is recommended. Precise tailoring of flaps combined with careful hemostasis and closure often renders drainage unnecessary.

C. *Splinting*.—Splinting of the postoperative stump serves two purposes: to restrain painful movements of the stump and to prevent contractures of joints. It also facilitates the application of snug bandaging. It is particularly important in leg amputations, in which the postoperative dressing should include a posterior splint from the upper thigh to a point several inches below the end of the leg stump.

D. *Physical Therapy*.—The amount and kind of physical therapy which may improve the function of an amputation stump depend on the type of amputation which has been performed and on the length of time which for one reason or another is allowed to elapse between the operation and the application of a permanent prosthesis. End bearing stumps may allow function in a permanent prosthesis within so few weeks that little treatment of the stump is needed. Stumps in which function of most of the remaining musculature is preserved will not shrink as much as stumps in which muscle atrophy of disuse is to be anticipated. Regular massage and the continuous wearing of a woven cotton elastic bandage serve to reduce the subcutaneous fat in a stump. Contrast baths, alcohol rubs and hot salt soaks are definitely useful in conditioning the skin and may be used as soon as the wound is healed. Early active motion preserves joint function and muscle tone. Splinting of joints between periods of exercise may be necessary to prevent contracture deformities. Healed

end bearing stumps should be given pressure exercises beginning within two weeks of amputation. In general the purpose is to begin active function, using some form of prosthesis at the earliest possible moment, and to apply such physical measures as may benefit the condition of the stump through the entire period until the patient is thoroughly accustomed to his permanent appliance.

4. THE TEMPORARY PROSTHESIS

Whenever possible the permanent prosthesis for an amputation should be planned and arranged for at the earliest practicable moment. Just as the duties of the surgeon performing an amputation as a life saving measure include the refashioning of the stump at a later date if necessary, so they include supervision of the

permanent socket can be fitted successfully. It also hastens the inevitable pressure atrophy caused by the use of an artificial limb. It is indicated only for the conical stump which may be inserted and withdrawn through the top of the socket. It does not meet the mechanical problems of alinement, weight bearing and motion, and its use may produce faulty habits difficult to correct after a permanent prosthesis has been fitted.

For below knee amputations a simple type of temporary prosthesis (fig. 2) can be obtained from the limb manufacturers at small cost, which is to be fitted to the patient's stump by means of a plaster of paris socket applied by the surgeon. This prosthesis is equipped with an articulated foot, movable knee joint and a canvas or leather thigh corset. In expert hands such prostheses

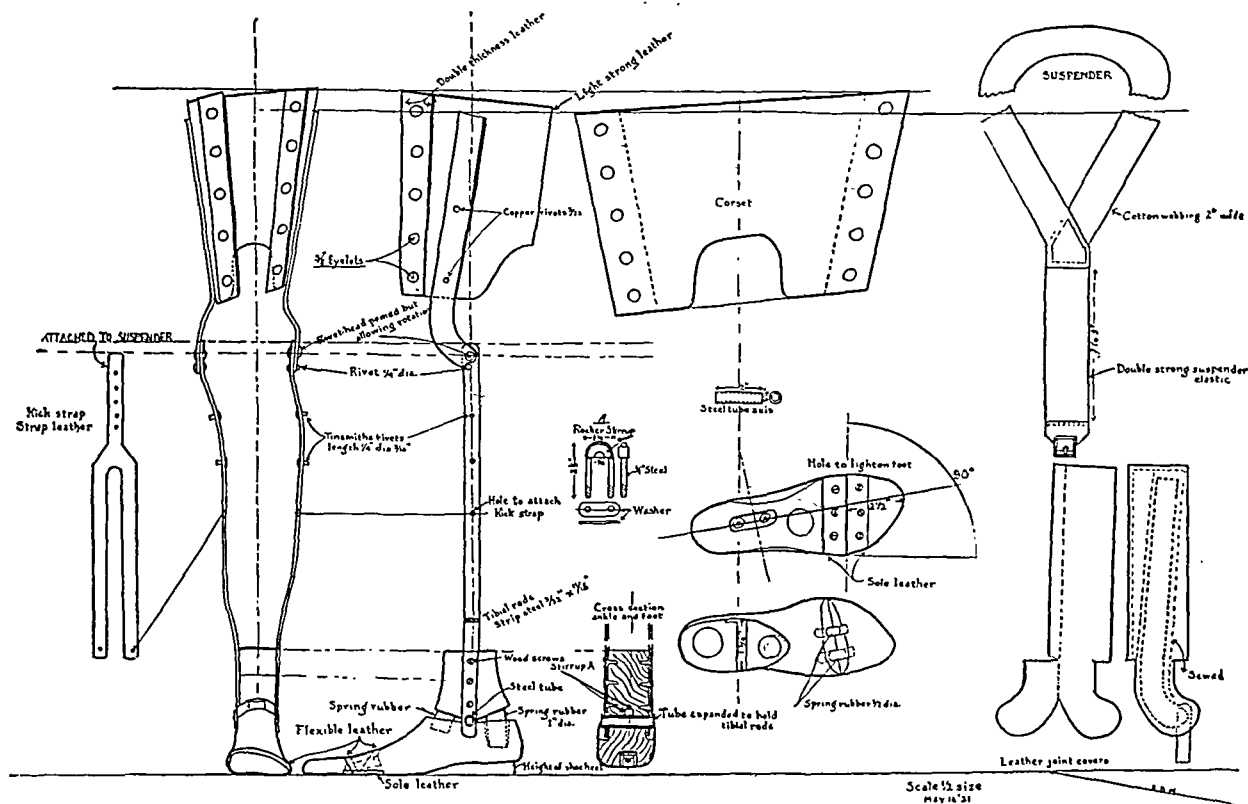


Fig. 2.—Diagram showing construction of skeleton leg for below-knee amputation.

patient until he has mastered the use of a permanent prosthesis. Unnecessary delay results not only in faulty psychologic adjustment and habits but in joint contracture and atrophy of the stump.

The degree of atrophy inevitable in an amputation stump depends largely on the amount of adipose tissue and functionless muscle tissue left in the stump. Nevertheless, all stumps shrink to a greater or less degree, and thus emerges the dilemma between the recognized advantages of early function and the objection that the original socket will no longer fit after the atrophy has occurred.

One escape from this dilemma is the use of a temporary pylon constructed by the surgeon, consisting of a plaster of paris socket lined with felt, mounted on a sawed off crutch and slung by straps from the shoulders or waist. This contrivance (fig. 1) rids the patient of the crutch habit at an early date, minimizes the contracture and wasting of the extremity from disuse, and reduces the bearing surface of the stump so that a

have frequently been fitted as early as from two to three weeks after amputation.

A third alternative is the use of a complete temporary prosthesis fitted by the limb manufacturer. Such an appliance might be expected to meet the requirements of alinement, motion and balance, but to do so makes its cost almost prohibitive. The provision of a temporary appliance at no charge aside from the cost of the permanent prosthesis has been used by some manufacturers as a method of sales promotion not beyond question from the ethical standpoint. A more salutary practice is the fitting of a permanent prosthesis at the earliest possible date, with the provision of a new socket within a few months if that becomes necessary when the inevitable atrophy has occurred. The cost of this method is relatively small.

In any case the prolonged "shrinking" of the stump by tight bandaging over many months is to be condemned. The advantage in permanent fitting is overshadowed by the physical and psychologic evils of disuse

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SATURDAY, NOVEMBER 23, 1940

IMMUNOLOGIC STUDIES OF POLIOMYELITIS

Numerous recent studies on the immunologic reactions of the poliomyelitis virus have resulted in a considerable extension of knowledge of its behavior. The expensive and somewhat cumbersome procedure of carrying out virus neutralization tests in monkeys to gain information which in most other infectious diseases could be derived from an equal number of test tubes or mice has resulted in efforts to devise a more satisfactory procedure. Recently Raffel and Schultz¹ endeavored to demonstrate a direct reaction between antigen and antibody along more practical lines. Their investigations were divided into four groups: experiments to demonstrate a reaction between virus and immune serums in vivo and in vitro, experiments to demonstrate a changed antigenic specificity of infected monkey cords in reactions with neutralizing serums and with anti-cord serums produced in rabbits, experiments on the obscure Schwartzman-Sanarelli reaction and studies on the heterogenic relationship between the virus or products of viral activity and the erythrocytes of various animal species. The studies involved a series of immunologic methods most of which had not been previously employed but all of which were aimed at eliciting a specific reaction based on an antibody or antigen derived from animals infected with poliomyelitis or convalescent. The technics employed included anaphylaxis in the guinea pig, the use of guinea pig and monkey uterine strips, cutaneous tests in monkeys and precipitative and complement fixation reactions. When the results were added to previous unsuccessful attempts to demonstrate specific precipitin, complement fixation and cutaneous reactions and to those experiments which have eliminated the possibility of the occurrence of a specific soluble antigen during the acute phase of the disease it was obvious that, aside from the neutralization test, the hope for a specific immunologic reaction for poliomyelitis is somewhat remote. Barring therefore the development of some more pro-

ductive line of research, reliance must continue to be placed on the virus neutralization test in spite of its disadvantages.

Successful adaptation of human poliomyelitis virus to the cotton rat and white mouse is one of the most promising advances in practical research technic of the present decade. Earlier apparently monkeys were the only susceptible animal species until Armstrong² reported transference of rhesus poliomyelitis virus to the eastern cotton rat. The disease thus produced in cotton rats was characterized by flaccid paralyses of the extremities associated with degenerative lesions of the anterior horn cells,³ these lesions being apparently identical with those usually observed in human poliomyelitis and in experimental poliomyelitis in monkeys. The identity of the rodent disease with rhesus poliomyelitis was further indicated by the fact that the rodent infection would produce typical poliomyelitic symptoms and lesions on return inoculation into monkeys.

It was afterward reported by Armstrong⁴ that the rhesus virus once serially adapted to the cotton rat could be successfully transferred to white mice. Proof of this transference, however, was incomplete, since it was found that the mouse virus was nonpathogenic on return inoculation into monkeys. This loss of pathogenicity suggested that the human poliomyelitis virus might have been lost, the observed symptoms in mice being due to some unknown neurotropic environmental virus. Such mouse viruses are known to be omnipresent in certain environments and have been recently studied in detail by Theiler⁵ and Olitsky.⁶

In order to complete the proof of the successful transference of the human virus to mice, Jungeblut and Sanders⁷ have more recently studied the antigenic properties of the passage virus directly isolated from the mouse brain and cord or after propagation in mouse tissue culture. Three successful mouse transferences of the SK New Haven strain of poliomyelitis virus were made by the Columbia University bacteriologists. Confirming earlier investigators, Jungeblut and Sanders found that on serial inoculation into the cotton rat the human virus rapidly lost its pathogenicity for monkeys. Simultaneously with this attenuation for the rhesus monkey there was an increase in rodent pathogenicity. Still further increases were noted in the mouse till a "fixed" virus was eventually obtained, wholly nonpathogenic for monkeys. This fixed virus could be successfully propagated in mouse tissue cultures, embryonic mouse brain in ox serum ultrafiltrate being the most effective culture medium.⁸

2. Armstrong, Charles: *Pub. Health Rep.* 54:1719 (Sept. 22) 1939.
3. Lillie, R. D., and Armstrong, Charles: *Pub. Health Rep.* 55:115 (Jan. 19) 1940.

4. Armstrong, Charles: *Pub. Health Rep.* 54:2302 (Dec. 29) 1939.

5. Theiler, Max: *J. Exper. Med.* 65:705 (May) 1937. Theiler, Max, and Gard, Sven, *ibid.* 72:79 (July) 1940.

6. Olitsky, P. K.: *J. Exper. Med.* 72:113 (Aug.) 1940.

7. Jungeblut, Claus W., and Sanders, Murray: *Proc. Soc. Exper. Biol. & Med.* 44:375 (June) 1940; *J. Exper. Med.* 72:407 (Oct.) 1940.

8. Sanders, Murray: *J. Exper. Med.* 71:113 (Jan.) 1940. Molloy, Eleanor: *Proc. Soc. Exper. Biol. & Med.* 44:563 (June) 1940.

1. Raffel, Sidney, and Schultz, E. W.: *Immunological Reactions in Poliomyelitis*, *J. Immunology* 39:265 (Oct.) 1940.

The immunochemical specificity of the fixed mouse (murine) virus was titrated against numerous specific antiviral serums. Serum-virus mixtures were incubated for ninety minutes at 37 C. and then titrated for unneutralized virus by serial intracerebral inoculations into white mice. Normal human, horse and monkey serums used as controls gave no suggestion of neutralization. Monkey convalescent serum, human convalescent serum and poliomyelitis immune horse serum gave partial or complete neutralization, the highest neutralizing titer being obtained with the pseudoglobulin fraction of homologous poliomyelitis immune horse serum. The serologic data presented by Jungeblut and Sanders leave little doubt that the human virus has been successfully transmitted and adapted to mice, by preliminary serial passage through monkeys and cotton rats.

The most encouraging results, however, have been the claimed successful immunization of monkeys by repeated subcutaneous injections with living mouse virus. This specifically attenuated viable murine vaccine is readily grown in artificial tissue cultures. While the immunity conferred by this viable vaccine is not absolute, it is sufficiently effective to stimulate optimism for further clinical research. If the Jungeblut murine vaccine should eventually prove to be clinically effective, Armstrong's initial observation of 1939 may prove to be one of the major discoveries of modern research medicine.

RHEUMATIC HEART DISEASE IN PHILADELPHIA HOSPITALS

Recently Hedley¹ of the United States Public Health Service reported the results of an extensive survey of cases of rheumatic heart disease in Philadelphia hospitals. This report covered a study of more than 4,600 cases of rheumatic heart disease, rheumatic fever, Sydenham's chorea and subacute bacterial endocarditis in hospitals of this area in the years 1930-1934 inclusive. Hedley's report includes an analysis of the age, race and sex distribution of the conditions mentioned as well as information on their interrelationship.

The importance of rheumatic heart disease as a problem of youth and early adulthood cannot be overemphasized. The onset in 69.1 per cent of the cases of rheumatic heart disease, as well as in 76.4 per cent of rheumatic fever and in 98.2 per cent of chorea, occurred before the age of 20 years. This large scale study shows, furthermore, that the peak of the onset of rheumatic fever, Sydenham's chorea and rheumatic heart disease occurred in the 5 to 9 year age period, the conditions being relatively uncommon in children under 5 years of age. Moreover, the onset of rheumatic fever and rheumatic heart disease in persons over 40 years of age was encountered in only a small percentage of cases. As indicated by Hedley, rheumatic heart disease, unlike some other types of heart disease, is not

a problem of great importance among older persons. The data with respect to more than 3,600 cases of rheumatic heart disease would tend to confirm the belief of most investigators that the condition is somewhat more common in females than in males, almost three fifths of the observed cases occurring in the female. This preponderance of cases in females was noted in all age groups except that of 15 to 19 years, in which period the number of cases in the two sexes was about equal. In agreement with most investigators, it was likewise noted that nearly twice as many cases of Sydenham's chorea were encountered in females as in males. About the same number of male and female patients were admitted for rheumatic fever.

About 13 per cent of patients with rheumatic heart disease were Negroes. Although this figure is in proportion to the size of the Negro population of Philadelphia, Hedley suggests that rheumatic heart disease is perhaps less common among Negroes than among white persons; owing to the less favorable economic status of the Negroes (50 per cent of the colored population being on relief) they are more likely to be hospitalized for rheumatic heart disease than are white persons. In any event a more extensive survey would be necessary to elucidate this point.

Observations made on the interrelation of rheumatic heart disease, rheumatic fever and Sydenham's chorea are interesting. Some 61 per cent of the cases of rheumatic heart disease included in the study gave histories of rheumatic fever or exhibited clinical manifestations of the latter condition, while Sydenham's chorea, with or without rheumatic fever, was indicated in slightly more than 15 per cent of the cases. Diagnoses indicated the presence of rheumatic heart disease in 42 per cent of the cases of Sydenham's chorea, and this figure would probably have been larger had the cases been followed after release from the hospital. Anyway these data, together with similar reports in the literature, indicate that the likelihood of developing rheumatic heart disease is much greater for a child with Sydenham's chorea than for one who has never had this condition. Almost 23 per cent of more than 3,600 cases of rheumatic heart disease, including cases complicated by subacute bacterial endocarditis, gave clinical evidence of rheumatic arthritis. More than 80 per cent of the patients under 20 years of age were regarded by Hedley as having active rheumatic infection. This investigator² has also pointed out that among persons under 30 years of age more than 75 per cent of the deaths from rheumatic heart disease are apparently attributable to active rheumatic infection.

Hedley's survey is particularly noteworthy because of the large number of cases on which it is based. It is restricted, however, to a single locality and might well be supplemented by similar extensive surveys made elsewhere. Thus the influence of factors peculiar to a restricted area would be as nearly as possible eliminated.

1. Hedley, O. F.: Rheumatic Heart Disease in Philadelphia Hospitals: II. Pub. Health Rep. 55: 1647 (Sept. 13) 1940.

2. Hedley, O. F.: Rheumatic Heart Disease in Philadelphia Hospitals: III. Pub. Health Rep. 55: 1707 (Sept. 20) 1940.

PAN AMERICAN HEALTH DAY

For nearly four decades the American republics have cooperated systematically in the prevention of the international spread of disease.¹ During the last two decades this cooperation has been made both more effective and extensive. In order to give this hemispheric relationship a more efficient and stable basis, the Pan American Sanitary Bureau was created in 1902. It is the oldest of the great international health bodies and practically the only one functioning at present.

Authority for the work of the bureau, which has grown from a purely advisory role in quarantine matters to an active interest in many health problems, is contained in the Pan American Sanitary Code adopted in Habana in 1924 and ratified by all the American republics, the first inter-American treaty to enjoy this distinction. During the years of its existence, the bureau has received constantly increasing support and financial assistance from the different republics.

Among the recent cooperative activities undertaken by the bureau² have been arrangements for international health conferences and representation at important meetings; health exhibits; organization of technical committees to study such problems as nutrition, malaria and health legislation; granting of scholarships; field work in plague control, poliomyelitis campaign, water supplies, sewage disposal, hospital organization, vital statistics, promotion of cultural relations; collection and dissemination of epidemiologic information; publication of the monthly bulletin and other literature including weekly statistics of disease prevalence; answering inquiries on public health and medical questions; furnishing aid in the case of catastrophes such as earthquakes; translating into Spanish the U. S. Pharmacopeia and allied material; distribution of bacterial cultures and biologic standards. Above all, however, stress has been laid on promotion of international cooperation in health matters and maintenance of relationship with various national health authorities.

In recognition of the success of these decades of inter-American health and medical cooperation, the fourth Pan American Conference of National Directors of Health resolved in May 1940 that Pan American Health Day should be celebrated every year in all the American republics. The date chosen for this purpose, December 2, was, in 1902, the date of the first Pan American Sanitary Conference in Washington. Decrees have already been issued in practically all the American republics proclaiming this day as Pan American Health Day. A similar proclamation is under consideration by the President of the United States, favorable action having been recommended by the Federal Security Administrator, the Secretary of State and the director of the Pan American Sanitary Bureau.

The celebration will have a twofold purpose: first, to commemorate what Pan American cooperation has achieved in health during the last few decades, recalling incidentally those great men who in all the American republics have done so much to promote public health and, second, to center attention on the teaching of preventive principles and practices and to rededicate all hearts to the great cause of public health and Pan Americanism. Elaborate arrangements have been made in practically all the American republics for the celebration of this day on a national scale, through the cooperation of health and educational authorities, national societies, the press, radio and similar agencies. Even outside its public health connections, the medical profession is going to take a leading part in the celebration. The academies of medicine of Colombia, Mexico and Peru are preparing official ceremonies. The plans for celebration in the United States include a radio program on December 2 in which representatives of leading medical and other scientific societies will participate.

Amid the troubles of this distracted world, all the nations in the American hemisphere, from the St. Lawrence River to Cape Horn, will unite in recalling the permanent blessings of peace and health. For this purpose international cooperation and understanding are essential. The physicians of the United States, who have always encouraged this movement for closer scientific relations among the American nations, will be pleased to join again in approval of this activity.

THIRD ANNUAL CONGRESS ON
INDUSTRIAL HEALTH

Industrial health is of exceptional interest at this time when national preparedness depends so greatly on industrial production. The attention of physicians is called to the program of the Annual Congress on Industrial Health published in the Organization Section in this issue. This will be the third of these meetings sponsored by the Council on Industrial Health of the American Medical Association. They are designed to acquaint the physician and others with the rapidly expanding importance of preventive medicine and surgery applied to industrial organization.

Since every man hour of production is vital at this time, the program of the congress is intended to be as helpful as possible to physicians called on to control those factors which in the past have contributed greatly to the incidence and costs of industrial absenteeism. In the field of trauma the hand and the eye have proved to be particularly vulnerable. Symposia have therefore been developed to present the best current opinion on the management of these costly forms of industrial disability. Of the occupational diseases, dermatitis has long been recognized as the most troublesome. A series of demonstrations has been planned to include discussion of the criteria for diagnosis of industrial cutaneous

1. The Tenth Pan American Sanitary Conference, editorial, J. A. M. A. 112:1258 (April 1) 1939.

2. Annual Report of the Director, Pan American Sanitary Bureau, 1939-1940.

disorders as well as accepted methods for the treatment and placement of susceptible employees. Among non-occupational diseases the common cold and influenza annually exact an enormous toll through loss of earning capacity and disruption of production schedules. This problem also will be discussed from the point of view of the essential economics, the possibilities of control through air conditioning and the role of the physician in industry and in private practice. Since many able-bodied men will probably be inducted into military service, industry may need to recruit workers from the physically handicapped and from the aging groups. These developments, of enormous medical and social significance, will be featured at the congress. Assignment of this type of worker into industry with proper consideration of physical ability and mental aptitude will be fully considered. Concern has been expressed about the availability of trained personnel in industrial health, the subject of an early resolution by the Committee on Medical Preparedness of the American Medical Association. A session will be devoted to determining what shortages exist and the best means for correction. It is hoped that concrete proposals for better training for the industrial nurse, the industrial hygienist, the safety engineer and the physician in industry may grow out of these discussions. A means will also be provided for the interchange of experience and results of recent activity by committees on industrial health in state and county medical societies.

The congress promises to provide an unusual opportunity to the medical profession to grasp a sense of its potential contribution to improved physical well-being among the employed population.

Current Comment

NARCOTIC PEDLERS IMPOSE ON PHYSICIANS' WIDOWS

From the Bureau of Narcotics in Washington comes a warning from the Commissioner, Mr. H. J. Anslinger, which should be widely disseminated among physicians and their families. Illicit traffickers in narcotics have in some instances recently developed a technic with which they were able to swindle either the widows or members of the families of physicians who had recently died. Apparently these peddlers watched the daily papers for the notices of deaths of physicians. Shortly after the publication of such a notice of death the trafficker appeared and represented himself to be "a narcotic appraiser," stating that he represented a federal agency and seeking to induce the survivors of the physician to turn over to him whatever narcotics might be found among the effects of the deceased. Thus far attempts have been made only on the families of physicians. It seems probable, however, that a similar attempt might be made in connection with stocks of narcotics held by druggists. Physicians and druggists everywhere should be warned against this type of fraud.

TUMORS IN TWINS

Macklin¹ recently appealed to physicians through medical journals for reports of cases of tumors in twins. Twenty case reports were thus obtained, seventeen of which had not been included previously in the literature. The author collected from the literature reports of fifty-three pairs of monozygous twins and thirty-five pairs of dizygous twins in which tumors occurred in either one or both twins. The newly discovered cases, together with those previously reported, were analyzed. It was found that tumors affect both members of a monozygous twin pair far more frequently than they affect both members of a dizygous twin pair. The tumor was of the same type and occurred in the same organ much more frequently in the monozygous than in the dizygous twin group. The age of onset of the tumors was more nearly identical in the monozygous than in the dizygous twins. The average difference in age of onset of the tumors in several pairs of identical twins in which both twins were affected was only 0.6 year, whereas in the fraternal twin pairs in which both twins were affected with tumors the average time elapsing between the ages of onset was 2.9 years, or five times as long. These observations appear to indicate that heredity plays an important part in tumor production and in the age of onset.

CARCINOGENIC LIPOID IN HUMAN CANCER

The extraction of a fat-soluble carcinogenic factor from primary breast cancer of man has been reported recently by Menke¹ of the Department of Surgery, Stanford University School of Medicine. Two primary carcinomas of the breast were excised by the Stanford surgeons, ground to a hash and subjected to repeated extraction with fat solvents in a Soxhlet apparatus. Acetone, ethyl ether, purified petroleum benzine and absolute ethyl alcohol were used in the order mentioned. The four extracts thus obtained from each tumor were pooled and evaporated to dryness, and samples of the resulting products were injected subcutaneously in the lower mammary region of virgin female mice. One tumor mass developed at the site of the injection in each series. The masses became palpable between the 229th and the 282d day and grew rapidly after this date, reaching about 2 cm. in diameter in from two to three weeks. At this stage each new growth was firmly adherent to and had already penetrated the abdominal walls. Gross metastases were not found. Histologically each tumor was a spindle cell sarcoma. Fragments transplanted to normal mice grew rapidly. Each transplant resulted in a 2 cm. ulcerating mass by the twentieth day. Spontaneous tumors failed to occur in 200 control mice during the course of the investigation. The chemical nature of this newly discovered human carcinogenic lipid and its possible antigenic properties are now under investigation.

1. Macklin, Madge Thurlow: An Analysis of Tumors in Monozygous and Dizygous Twins, with a Report of Fifteen Unpublished Cases, *J. Heredity* **31**: 277 (June) 1940.

1. Menke, J. F.: *Science* **92**: 290 (Sept. 27) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

THE NAVAL RESERVE

The Secretary of the Navy has stated that naval reservists are serving in practically every type of ship of the fleet and in administrative duties ashore. Since the emergency proclamation by the President, Sept. 8, 1939, the officers and men of the Naval Reserve, excepting men of the Fleet Reserve, have reported for duty on a voluntary basis. The rapid acquisition of ships for auxiliaries, patrol and harbor defense duties necessitated, however, placing the organized Naval Reserve on a compulsory basis, which the Secretary of the Navy did October 5. The Navy Department indicated that, as of Oct. 26, 1940, 2,500 Naval Reserve officers of all classes were on duty and 4,000 enlisted men, not including the Fleet Reserve.

The Naval Reserve has numerous projects under way at this time, giving officers and men special training, with active duty available for all candidates who volunteer on completion of the courses. Among the classes for officers are flight aviation medicine at Pensacola, Fla., supply corps school at Washington, D. C., chemical warfare school at Edgewood Arsenal, Maryland, industrial procurement at the Army War College, merchant marine training centers in New York and San Francisco, the harbor defense school at Boston, for the training of engineer officers of organized divisions assigned to local defense duties and the Naval Reserve midshipmen schools, aboard the U. S. S. *Illinois*, New York, and at Abbott Hall, Northwestern University, Chicago. The last two schools are part of the Navy's program to train approximately 4,000 line ensigns of the Naval Reserve qualified for duty afloat. A third school will be opened at the Naval Academy in February 1941.

MEDICAL SUPPLIES FOR ENGLAND

The Medical and Surgical Supply Committee of America, with headquarters at 420 Lexington Avenue, New York, comprising 265 physicians throughout the United States, was formed last August to secure medical supplies to be sent overseas for aid to the civilian population in England. The committee announces that already more than \$40,000 in medical and surgical supplies has been shipped abroad. Among the supplies donated were a portable x-ray machine, a portable anesthesia unit, five barrels of surgical instruments, diamond earrings valued at \$1,000 to be converted into cash to purchase medical equipment, and an operating kit valued at \$400. Druggists and pharmaceutical and supply houses have sent thousands of hypodermic needles valued at \$7,000, Luer syringes, large quantities of bandage, drugs, hundreds of surgeon's gloves, and other valuable equipment.

Another organization, Bundles for Britain, Inc., 29 West 57th Street, New York, has formed a medical and surgical supply department, but it is in no way affiliated with the Medical and Surgical Supplies Committee of America, the executive chairman of which is

Mrs. Ronald B. Balcom. The sole function of the Medical and Surgical Supply Committee of America is to assemble medical supplies and instruments from donors, to inspect the material, restore the surgical instruments, and then ship them abroad for use in emergency hospitals and field units in Great Britain.

OHIO CHIEF OF SELECTIVE SERVICE

Dr. Howard E. Boucher, Columbus, lieutenant colonel and executive officer of the 112th Medical Regiment, Ohio National Guard, has been appointed chief medical officer of Selective Service in Ohio. There will be three medical induction centers in Ohio: Fort Hayes at Columbus, and at Toledo and Cleveland. The Committee on Medical Preparedness has furnished to the governor a list of qualified physicians for positions as medical examiners and alternate examiners for the 330 local draft boards.

NATIONAL DEFENSE NIGHT

The program of the Philadelphia County Medical Society, Philadelphia, November 13, was devoted to national defense. The speakers were Dr. William DeKleine, Washington, D. C., medical director, American Red Cross, on "Red Cross Participation in Medical Defense"; Brig. Gen. Leigh C. Fairbank, chief, Dental Corps, U. S. Army, Washington, D. C., "The Part Dentists Play in National Defense," and Rear Admiral Adolphus E. Watson, commandant, Fourth Naval District, Philadelphia, "The Navy Ashore." Certificates were conferred on members in practice for fifty years. The program was presented in collaboration with the W. W. Keen chapter, Association of Military Surgeons of the United States.

LECTURES ON MILITARY MEDICINE

Recent lectures in the series on military medicine sponsored by the Philadelphia County Medical Society are as follows:

Dr. Isidor S. Ravdin, *Advances in Therapeutics as Related to War Surgery*, October 17.

Major James B. Mason, Medical Corps, U. S. Army, *Tissue Reaction to Missiles of War—Ballistics*; also Dr. William Bates, *The Surgery of War as Contrasted with Industrial Surgery*, October 24.

Dr. Robert H. Ivy, *Maxillofacial and Reconstructive Surgery in War*, October 31.

Dr. Max M. Strumia, *Transfusions of Blood and Hematologic Substitutes in Advanced Medical Installations in War*, November 7.

The present series of thirteen lectures ends early in December; another series will follow shortly thereafter.

The society recently reported that 1,212 questionnaires have been returned to its office from those sent out to obtain data concerning availability of local phy-

sicians for service in the event of a national emergency. Of this number 729 were from members of the society and 483 from nonmembers. There are about 4,200 physicians in Philadelphia, it was pointed out.

AMERICAN MOBILIZATIONS

According to a statistical study made by the U. S. Veterans' Administration, Washington, D. C., America mobilized 350,000 men for the American Revolutionary War, 527,650 for the war of 1812, 107,631 for the war with Mexico, 2,128,948 (Union forces only) for the Civil War, 280,564 for the Spanish-American War, 130,000 for the Indian wars and 4,791,172 for the World War. The average age of the World War

doughboy, according to the Associated Press in commenting on the foregoing statistics, is now 47 years and of the Spanish-American veteran 65. The Civil War campaigner averages 95. The Veterans' Administration statistical study shows that 4,041,017 World War veterans were living at the beginning of 1940.

PSYCHIATRIC PROBLEMS

A symposium on psychiatric problems concerning military conscription was presented before the Medical Society of St. Elizabeths Hospital, Washington, October 22; the speakers were Capt. Dallas G. Sutton, U. S. Navy, Lieut. Col. William C. Porter, U. S. Army, and Dr. Harry Stack Sullivan.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

FIRST CORPS AREA

The following medical reserve officers have been ordered to extended active duty with the regular army by headquarters of the First Corps Area, which comprises the states of Maine, Massachusetts, Connecticut, New Hampshire, Vermont and Rhode Island:

ALLEN, Eugene E., 1st Lieut., Milford, Mass.
ALPERT, George R., 1st Lieut., Brookline, Mass.
ANDERSON, Karl V., 1st Lieut., Derby, Maine.
ANDREN, Henry E., 1st Lieut., Boston.
ASCHER, David S., 1st Lieut., Boston.
BACHRACH, Samuel, 1st Lieut., Maynard, Mass.
BARALD, Fred C., 1st Lieut., New Haven, Conn.
BOYER, Samuel H., 1st Lieut., Winchester, Mass.
BURKE, Jacob B., 1st Lieut., Chelsea, Mass.
CARPENTIERI, Anthony L., 1st Lieut., New Haven, Conn.
CASERTA, Silvio J., 1st Lieut., Bridgeport, Conn.
CLOUGH, Herbert T. Jr., 1st Lieut., Bangor, Maine.
CORCORAN, John J., 1st Lieut., West Roxbury, Mass.
DONAGHY, George E., 1st Lieut., Boston.
DORFMAN, Jacob, 1st Lieut., Hartford, Conn.
EGAN, William J., 1st Lieut., Dorchester, Mass.
FICICCHY, John Jr., 1st Lieut., Hyde Park, Mass.
FOLEY, John J., 1st Lieut., Malden, Mass.
FOX, Lester I., 1st Lieut., Quincy, Mass.
FREEDMAN, Stanley S., 1st Lieut., Providence, R. I.

GARDINER, Harry M., 1st Lieut., Harding, Mass.
GOLDMAN, Max, 1st Lieut., Boston.
GRIFFIN, Julian P., 1st Lieut., Indian Orchard, Mass.
HEIFETZ, Ralph, 1st Lieut., Portland, Maine.
HYDE, Robert W., 1st Lieut., Fairfax, Vt.
JACOBS, Harry, 1st Lieut., Concord, Mass.
JOHNSON, Paul E., 1st Lieut., Attleboro, Mass.
KASPARIAN, Karl D., 1st Lieut., Dorchester, Mass.
LEVINE, Samuel, Captain, Lynn, Mass.
McCABE, George E., 1st Lieut., Arlington, Mass.
McCARTHY, Robert J., 1st Lieut., Dorchester, Mass.
McWETHY, Wilson H., 1st Lieut., Augusta, Maine.
MERLIN, Samuel A., Captain, Dorchester, Mass.
MOSKOVITZ, Abraham J., 1st Lieut., Burlington, Vt.
ROBEY, Nathaniel C., Captain, Newton Centre, Mass.
ROGELL, David, 1st Lieut., Warren, R. I.
ROSEN, Daniel, 1st Lieut., Roxbury, Mass.
RUBIN, Abraham, 1st Lieut., Pittsfield, Mass.
RUBINO, Bernard C., 1st Lieut., Baldwinsville, Mass.
SILVER, Gershon B., 1st Lieut., Hartford, Conn.
SINCLAIR, Edmond B., 1st Lieut., Providence, R. I.
STANKARD, William F., 1st Lieut., Stamford, Conn.
SWANN, William K. Jr., 1st Lieut., Boston.
TEMPLE, Francis E., 1st Lieut., Providence, R. I.
THOMAS, John M. Jr., 1st Lieut., Woodstock, Vt.
WIENER, Harry J., 1st Lieut., Revere, Mass.
WIEMERS, Eugene L., 1st Lieut., Concord, N. H.
ZELTZERMAN, Israel, 1st Lieut., Foxboro, Mass.

THIRD CORPS AREA

The following medical reserve corps officers have been ordered to extended active duty by the commanding general of the Third Corps Area, which includes the states of Pennsylvania, Virginia, the District of Columbia and Maryland:

BOYCE, Bingham, Captain, Bridgeville, Pa.
BRYLAWSKI, Michael, 1st Lieut., Philadelphia.
BUSH, Herman, 1st Lieut., Beaver Falls, Pa.
CARROLL, Edward Joseph, Jr., Captain, Pittsburgh.
COHEN, Max Harry, 1st Lieut., Washington, D. C.
COVALESKY, Victor John, 1st Lieut., Allentown, Pa.
DIXON, Joseph Moore, Captain, Roanoke, Va.
DELP, Charles William, Captain, St. Clair, Pa.
ERHARD, Elmo Enos, Captain, Curwensville, Pa.
FLUEGEL, Gerald Nicholas, Captain, Wilkes-Barre, Pa.
GERWIG, Walter Henry, Jr., 1st Lieut., Baltimore.
GORDON, Armand Byron, 1st Lieut., Washington, D. C.

HARRISON, Malcolm D., 1st Lieut., Washington, D. C.
JANJIGIAN, Edward Rupen, 1st Lieut., Danville, Pa.
KIRK, Milo Miller, 1st Lieut., Pittsburgh.
MANSFIELD, William Kenneth, 1st Lieut., Baltimore.
MASON, James B., Major, Philadelphia.
McLAUGHLIN, William B., Captain, Pittsburgh.
MILLIGAN, Alexander McLeod, Lieut. Col., Pittsburgh.
MOGAN, Christopher Joseph, Captain, Philadelphia.
SCHUBART, George Rudolph, 1st Lieut., Drexel Hill, Pa.
SHOWALTER, Josiah Thomas, 1st Lieut., Cambria, Va.
SONES, Maurice, 1st Lieut., Philadelphia.
STEIN, Arthur Julian, 1st Lieut., Philadelphia.
THOMAS, Preston Whitney, 1st Lieut., Pittsburgh.
TOLSTOI, George, 1st Lieut., Washington, D. C.
UHDE, George Irvin, 1st Lieut., Kennett Square, Pa.
URBAITIS, John Charles, Captain, Frankford, Pa.
VAN BUSKIRK, Frederick William, 1st Lieut., Pottstown, Pa.
WEST, George Brooks, Lieut. Col., Norfolk, Va.
WHITE, George Seese, 1st Lieut., Uniontown, Pa.
YINGLING, Paul Louis, 1st Lieut., Shippensburg, Pa.

FOURTH CORPS AREA

The following medical reserve corps officers have been ordered to extended active duty by the commanding general of the Fourth Corps Area, which includes the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana. Their rank, home address and station are indicated.

AARON, George, 1st Lieut., New Orleans, Camp Blanding, Fla.
ADAMS, Edward N., Captain, Florence, S. C., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
ASKEW, Rufus A., 1st Lieut., Atlanta, Ga., Fort Bragg, N. C.
ASKEW, William M. Jr., 1st Lieut., Greenville, Ala., Camp Blanding, Fla.

ASKIN, Henry E., 1st Lieut., Alexander City, Ala., Camp Shelby, Miss.
BATEMAN, Needham B., Captain, Atlanta, Ga., Rctg. Serv., Atlanta, Ga.
BECK, Chester K., 1st Lieut., Troy, Ala., Fort Screven, Ga.
BENNETT, Basil T. Jr., 1st Lieut., Trenton, Tenn., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
BENTON, George R., 1st Lieut., Goldsboro, N. C., Camp Beauregard, La.
BERMAN, Maxwell D., Captain, Jackson, Miss., Camp Shelby, Miss.
BLUMBERG, Max N., 1st Lieut., Macon, Ga., Fort Jackson, S. C.
BOLLING, Harlis O., 1st Lieut., Kingsport, Tenn., C. A. Laboratory, Fort Benning, Ga.
BOS, Howard C., 1st Lieut., Waycross, Ga., Fort Jackson, S. C.
BOYKIN, James T., 1st Lieut., Lewisburg, Tenn., 9th Div., Fort Bragg, N. C.
BRABHAM, Vance W. Jr., 1st Lieut., Augusta, Ga., Fort Bragg, N. C.

- BRACKSTONE, LeRoy B., 1st Lieut., Iuka, Miss., 8th Div., Fort Jackson, S. C.
- BRAMLETT, Eugene V., 1st Lieut., Oxford, Miss., Fort Jackson, S. C.
- BROOKS, Marshall J. Jr., 1st Lieut., Atlanta, Texas, Fort McClellan, Ala.
- BRUTON, Ogden C., Captain, Nashville, Tenn., Fort McClellan, Ala.
- BRYAN, Malvern T., 1st Lieut., Memphis, Tenn., Fort Jackson, S. C.
- BRYAN, Phillips R., 1st Lieut., Reynolds, Ga., Fort Oglethorpe, Ga.
- BURDINE, Winston E., 1st Lieut., Marble Hill, Ga., 8th Div., Fort Jackson, S. C.
- BURKETT, Howard M., 1st Lieut., Memphis, Tenn., Camp Beauregard, La.
- BUSH, James LeSesne, Captain, Dublin, Ga., Retg. Serv., Memphis, Tenn.
- CAMPBELL, Edmond C., 1st Lieut., Morganza, La., Camp Shelby, Miss.
- CAMPBELL, Guy, 1st Lieut., Jena, La., Fort Bragg, N. C.
- CARNEY, Henry M., Captain, Nashville, Tenn., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- CARTER, Thomas S., Captain, Miami, Fla., Fort Bragg, N. C.
- CHAPMAN, Jules B., 1st Lieut., Jacksonville, Fla., Fort Bragg, N. C.
- CHESSON, Andrew L., 1st Lieut., Elizabeth City, N. C., Camp Beauregard, La.
- CHILTON, Alfred M., 1st Lieut., Anniston, Ala., 4th Div., Fort Benning, Ga.
- COMEK, Edward T., Captain, Eufula, Ala., Camp Beauregard, La.
- COOPER, Charles F. Jr., 1st Lieut., Macon, Ga., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- COYLE, Daniel J., 1st Lieut., Birmingham, Ala., Camp Shelby, Miss.
- COYLE, Elda S., 1st Lieut., Plain Dealing, La., Fort McClellan, Ala.
- CRAIGHEAD, Claude C., 1st Lieut., Athens, Ga., Camp Blanding, Fla.
- CREE, Maurice B., 1st Lieut., Concord, N. C., Camp Shelby, Miss.
- DABNEY, William M., 1st Lieut., Okolona, Miss., Fort Jackson, S. C.
- DALE, Sebron C., 1st Lieut., Jackson, Miss., Camp Beauregard, La.
- DARDEN, William H., 1st Lieut., Birmingham, Ala., Fort McClellan, Ala.
- DARNALL, Robert M., 1st Lieut., Union City, Tenn., Camp Shelby, Miss.
- DAVIS, Julian W., 1st Lieut., Birmingham, Ala., Fort Benning, Ga.
- DELEO, Caesar A., 1st Lieut., New Orleans, Camp Beauregard, La.
- DIAZ, Walter P., 1st Lieut., New Orleans, Camp Shelby, Miss.
- DYER, John D., 1st Lieut., Van Vleet, Miss., Fort Bragg, N. C.
- EDWARDS, Arthur M., 1st Lieut., Bernice, La., Camp Beauregard, La.
- EDWARDS, Elbert E. Jr., 1st Lieut., Bells, Tenn., Camp Beauregard, La.
- EGLESTON, Joseph D. Jr., 1st Lieut., Old Hickory, Tenn., Camp Shelby, Miss.
- ELLINGTON, Joseph C., 1st Lieut., Alto, La., Fort Jackson, S. C.
- ELLIS, Edward W., 1st Lieut., Knoxville, Tenn., Camp Shelby, Miss.
- FEDER, Alexander J., 1st Lieut., Franklinton, La., Camp Shelby, Miss.
- FEDUCIA, Samuel J., 1st Lieut., Cotton Valley, La., Camp Beauregard, La.
- FENDLER, Benny, 1st Lieut., Memphis, Tenn., Camp Beauregard, La.
- FENBERG, Henry H., 1st Lieut., New Orleans, Camp Shelby, Miss.
- FITTS, William L. III, 1st Lieut., New Orleans, Camp Blanding, Fla.
- FRANKEL, David E., 1st Lieut., Waycross, Ga., Camp Blanding, Fla.
- FREEDMAN, Harold D., 1st Lieut., Senatobia, Miss., Fort McClellan, Ala.
- GARLAND, William J., 1st Lieut., Logansport, La., Camp Beauregard, La.
- GILREATH, Robert A., Captain, Henderson, N. C., Fort Bragg, N. C.
- GLASSBERG, Irving J., 1st Lieut., New Orleans, Camp Shelby, Miss.
- GLASS, Thomas A. Jr., 1st Lieut., Shreveport, La., Fort McClellan, Ala.
- GLAZER, Harry, 1st Lieut., Montgomery, Ala., Retg. Serv., New Orleans.
- GLISSON, Charles S. Jr., Captain, Atlanta, Ga., Fort Bragg, N. C.
- GOLDSTEIN, Nathan, 1st Lieut., New Orleans, Camp Blanding, Fla.
- GRACE, Kenneth D., 1st Lieut., La Grange, Ga., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- GREEN, Albert H., Captain, Birmingham, Ala., Camp Beauregard, La.
- GWIN, John V., 1st Lieut., New Orleans, Fort Barrancas, Fla.
- HAIR, Morris J., Captain, LeCompte, La., Camp Beauregard, La.
- HANAHAN, Ralph B., 1st Lieut., Florence, S. C., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- HARLOW, John R., 1st Lieut., Jonesboro, La., 4th Div., Fort Benning, Ga.
- HARMON, James P., 1st Lieut., Quincy, Fla., 4th Div., Fort Benning, Ga.
- HART, William W., 1st Lieut., Riggold, La., Camp Beauregard, La.
- HARVEY, Robert H., Captain, Erwin, Tenn., Fort Oglethorpe, Ga.
- HASSETLINE, Lee L., 1st Lieut., Carville, La., Fort Oglethorpe, Ga.
- HAWES, James B., 1st Lieut., Greenville, N. C., Fort Benning, Ga.
- HEAD, Homer Jr., 1st Lieut., Chattanooga, Tenn., Fort Jackson, S. C.
- HEATH, Rudolph W., 1st Lieut., Tampa, Fla., Fort Jackson, S. C.
- HEMBREE, John A., Captain, Jeffersonville, Ga., Camp Shelby, Miss.
- HENDRIX, Richard W., Captain, Evergreen, Ala., Camp Shelby, Miss.
- HENSHALL, George K. Jr., 1st Lieut., Chattanooga, Tenn., Fort Moultrie, S. C.
- HERAULT, Pierre C. Jr., 1st Lieut., Atlanta, Ga., 2d Armored Div., Fort Benning, Ga.
- HILL, OTHO R., Captain, Lebanon, Tenn., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- HOGAN, Cecil M., 1st Lieut., Jacksonville, Fla., 8th Div., Fort Jackson, S. C.
- HOLDEN, Howard T., 1st Lieut., Rabun Gap, Ga., Army Medical Center, Washington, D. C.
- HOOVER, William M. Jr., 1st Lieut., Coral Gables, Fla., Camp Shelby, Miss.
- HOPKINS, George S., 1st Lieut., Lake Providence, La., Camp Shelby, Miss.
- HOWELL, Robert P., Captain, Lake Charles, La., Camp Beauregard, La.
- HUMBERT, Walter C., Captain, Erwin, Tenn., Camp Beauregard, La.
- HUNTER, John W. Jr., 1st Lieut., Birmingham, Ala., Camp Blanding, Fla.
- IRWIN, Thomas M., 1st Lieut., Orlando, Fla., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- JAMES, Lorenzo, 1st Lieut., Haynesville, Ala., Camp Blanding, Fla.
- JAMISON, Andrew M. Jr., 1st Lieut., Spartanburg, S. C., Fort Jackson, S. C.
- JOHNSTON, William O., 1st Lieut., Charlotte, N. C., Camp Shelby, Miss.
- KIMMELL, William F., 1st Lieut., Memphis, Tenn., Camp Shelby, Miss.
- KNIGHTON, James E., 1st Lieut., Shreveport, La., Fort McClellan, Ala.
- KUSHNER, Louis Z., Captain, Lake Charles, La., Camp Beauregard, La.
- LABARGE, Oza J., 1st Lieut., New Orleans, Camp Beauregard, La.
- LANASA, Matthew J., 1st Lieut., Baton Rouge, La., Camp Peay, Tulahoma, Tenn.
- LARY, John H., 1st Lieut., Huntsville, Ala., 4th Div., Fort Benning, Ga.
- LEIDENHEIMER, Henry Jr., 1st Lieut., New Orleans, Camp Shelby, Miss.
- LEWIS, Arthur N., 1st Lieut., Mobile, Ala., 4th Div., Fort Benning, Ga.
- LUCAS, Robert L., Captain, Winfield, Ala., Fort McClellan, Ala.
- MCCARN, Dan W., 1st Lieut., Warrior, Ala., Camp Shelby, Miss.
- MCCCLARY, George R., 1st Lieut., Miami, Fla., Camp Peay, Tenn.
- MCCONNELL, Hiram A., 1st Lieut., Bunkie, La., Camp Shelby, Miss.
- McELWEE, Newell E. Jr., 1st Lieut., Crowley, La., Camp Beauregard, La.
- McGINNIS, Perry A., Captain, Bean Station, Tenn., Retg. Serv., Knoxville, Tenn.
- McGINTY, Howard C., 1st Lieut., Statesboro, Ga., 8th Div., Fort Jackson, S. C.
- McVEA, Charles, 1st Lieut., Baton Rouge, La., Fort Moultrie, S. C.
- MAJURE, Ernest O., 1st Lieut., Wetumka, Ala., Camp Blanding, Fla.
- MARTIN, Farris J., 1st Lieut., Montgomery, Ala., Camp Shelby, Miss.
- MASSENGILL, Robert C., 1st Lieut., Brookhaven, Miss., Camp Shelby, Miss.
- MAY, William P., 1st Lieut., Winston-Salem, N. C., Fort McClellan, Ala.
- MELCHER, Willis A., 1st Lieut., Wilson, N. C., Camp Blanding, Fla.
- MERRIAM, Lucius B., 1st Lieut., Waynesboro, Miss., Camp Blanding, Fla.
- MINOR, Walter H. Jr., Captain, Mobile, Ala., Camp Beauregard, La.
- MONSKY, David B., 1st Lieut., Montgomery, Ala., Retg. Serv., Montgomery, Ala.
- MYERS, Onnie P., 1st Lieut., Indianola, Miss., Fort McClellan, Ala.
- NEWELL, Charles E., Captain, Pineville, La., Fort Jackson, S. C.
- NOBLE, William, 1st Lieut., Attalla, Ala., Fort McClellan, Ala.
- NORTON, John W. R., Captain, Chapel Hill, N. C., Fort Bragg, N. C.
- NOTO, Joseph J., 1st Lieut., Baton Rouge, La., 9th Div., Fort Bragg, N. C.
- OLIVER, Ernest B., 1st Lieut., Birmingham, Ala., Camp Shelby, Miss.
- OLSON, John R., 1st Lieut., Nashville, Tenn., Camp Blanding, Fla.
- OWINGS, Franklin D., 1st Lieut., Rockwood, Tenn., Camp Beauregard, La.
- PARKS, Richard H., 1st Lieut., Cross Hill, S. C., Camp Shelby, Miss.
- PAULLUS, George E. Jr., Captain, Memphis, Tenn., Camp Shelby, Miss.
- PHILLIPS, James R., 1st Lieut., Baton Rouge, La., Camp Blanding, Fla.
- PHILLIPS, Stonewall J., Captain, Oakdale, La., Fort Jackson, S. C.
- PLOTKIN, Oscar M., 1st Lieut., Columbia, S. C., Fort Bragg, N. C.
- PRICE, Vivian H., 1st Lieut., Shreveport, La., Fort Bragg, N. C.
- PRITCHARD, Clarence D., 1st Lieut., Marks, Miss., Camp Shelby, Miss.
- RAY, Emmett B., 1st Lieut., Kosciusko, Miss., Camp Beauregard, La.
- RICHARD, GOLDEN G., 1st Lieut., Lake Arthur, La., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- RING, Harold H., Captain, Savannah, Ga., Fort Screven, Ga.
- RING, Louis J., 1st Lieut., Mount Olive, N. C., Camp Shelby, Miss.
- ROANE, Henry S. Jr., 1st Lieut., Ruston, La., Camp Shelby, Miss.
- ROBERTS, Roy F., 1st Lieut., Asheville, N. C., Camp Shelby, Miss.
- ROBINSON, John F., 1st Lieut., Anderson, S. C., Camp Shelby, Miss.
- ROBINSON, Robert L., 1st Lieut., Mars Hill, N. C., Camp Blanding, Fla.
- ROBSON, Frank Y., 1st Lieut., Tampa, Fla., Fort Jackson, S. C.
- ROGERS, James T., Captain, Gainesville, Ga., 4th C. A. Hdqrs., Atlanta, Ga.
- RUDD, James C., Captain, Greensboro, N. C., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- SASLAW, Milton S., Captain, Miami, Fla., Camp Shelby, Miss.
- SCHMIDT, Henry L. Jr., 1st Lieut., Brunswick, Ga., 8th Div., Fort Jackson, S. C.
- SCOTT, Wood H., 1st Lieut., Bonita, La., Fort McClellan, Ala.
- SHELTON, James B., 1st Lieut., Bessemer, Ala., Camp Shelby, Miss.
- SHULL, Harrison J., Captain, Shelbyville, Tenn., 8th Div., Fort Jackson, S. C.
- SIMMONS, Shelton C. Jr., 1st Lieut., East Point, Ga., Camp Beauregard, La.
- SLAUGHTER, William J., 1st Lieut., DeKalb, Miss., Camp Beauregard, La.
- SMITH, Jack I., 1st Lieut., Mooresville, Ala., Camp Blanding, Fla.
- SNELLING, David B., 1st Lieut., Eutaw, Ala., Fort Jackson, S. C.
- STANDER, Leonard H., 1st Lieut., Istrouma, La., Camp Shelby, Miss.
- STEWART, Williams D., 1st Lieut., Ooltewah, Tenn., Fort Benning, Ga.
- STEWART, John R., 1st Lieut., Minden, La., Camp Blanding, La.
- SULLIVAN, Joseph T., 1st Lieut., Asheville, N. C., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- SWEARINGEN, David C., Captain, Shreveport, La., Camp Shelby, Miss.
- TAYLOR, Guy F., 1st Lieut., Laurel Springs, Tenn., Savannah Anti-Aircraft Firing Center, Savannah, Ga.
- THOMAS, William C., Captain, Shier City, N. C., Fort Bragg, N. C.
- TOPP, Olvert W., 1st Lieut., Greenville, S. C., Fort Bragg, N. C.

UNDERWOOD, James W., 1st Lieut., Birmingham, Ala., Camp Beauregard, La.
VOORHIES, Norton W., 1st Lieut., New Orleans, La., 9th Div., Fort Bragg, N. C.
WARREN, John B., 1st Lieut., Piney Flats, Tenn., 4th Div., Fort Benning, Ga.
WARSHAUER, Samuel E., 1st Lieut., Wilmington, N. C., Camp Shelby, Miss.
WATSON, James E., 1st Lieut., Memphis, Tenn., Camp Beauregard, La.
WEBB, John K., 1st Lieut., Columbia, S. C., 4th Div., Fort Benning, Ga.
WEINBERGER, Jacob, 1st Lieut., Jamestown, Tenn., Rctg. Serv., Jackson, Miss.
WEINREB, Joseph, Captain, Jacksonville, Fla., Rctg. Serv., Jacksonville, Fla.
WELLS, James H., 1st Lieut., Ruston, La., Fort Bragg, N. C.

WHITE, William E., 1st Lieut., Anniston, Ala., Fort McClellan, Ala.
WILKINSON, Charles F. Jr., 1st Lieut., Atlanta, Ga., Fort Jackson, S. C.
WILLIAMS, Alton F., 1st Lieut., Metter, Ga., Fort Jackson, S. C.
WILLIAMS, John W., 1st Lieut., Greenville, Miss., Camp Blanding, Fla.
WILLIEN, Leon J., Captain, Knoxville, Tenn., Camp Blanding, Fla.
WILSON, James R., 1st Lieut., Thomson, Ga., Fort Jackson, S. C.
WINDHAM, John E., 1st Lieut., Kosciusko, Miss., Camp Shelby, Miss.
WOOD, Frank A., 1st Lieut., Monroe, La., Fort Oglethorpe, Ga.
WOODRUFF, Gerald G., Captain, Anniston, Ala., Fort McClellan, Ala.
WORD, Samuel B., 1st Lieut., Birmingham, Ala., Camp Shelby, Miss.
WYATT, Thomas E., 1st Lieut., Union City, Tenn., Camp Beauregard, La.
YOUNG, George G., LaFayette, Ga., Fort Jackson, S. C.
ZALIN, Jacob, 1st Lieut., Walterboro, S. C., Fort Jackson, S. C.

SIXTH CORPS AREA

The following medical reserve corps officers in the Sixth Corps Area, which comprises Illinois, Wisconsin and Michigan, had been ordered by the Corps Area Commander to extended active duty up to November 8:

BALDWIN, Robert S., Captain, Marshfield, Wis.
BLOOM, Norman B., 1st Lieut., Milwaukee.
BROWN, Carroll A., 1st Lieut., Lincoln, Ill.
BUCZYNSKI, Charles C., Captain, Chicago.
BULMER, Dan J., 1st Lieut., Ann Arbor, Mich.
BURKHART, Jean M., 1st Lieut., Benton, Ill.
CASTRO, Cosimo, 1st Lieut., Chicago.
CAVELL, Roscoe W., Captain, Eloise, Mich.
CUNNINGHAM, Glenn D., 1st Lieut., Rock Island, Ill.
DISKIN, Herman E., 1st Lieut., Detroit.
DULIN, Theodore J., 1st Lieut., Kankakee, Ill.
EISELE, Paul L., Captain, Statesan, Wis.
ELLWOOD, Walter W., Captain, Chicago.
ERENBURG, Leon M., Captain, Chicago.
FARBER, Charles E., 1st Lieut., Grand Rapids, Mich.
GORDON, Hymen S., Captain, Coal City, Ill.
GOSS, Samuel B., 1st Lieut., Ann Arbor, Mich.
GRAY, Arthur S., 1st Lieut., Allen Park, Mich.
GREENBERG, Leo J., 1st Lieut., Chicago.
HELM, John E., 1st Lieut., Benton, Ill.
HICK, Ford K., Captain, Oak Park, Ill.
HOWE, George E., 1st Lieut., Francis Creek, Wis.

ILLYES, Roscoe O., 1st Lieut., Chicago.
JEROME, Bourne, Captain, Superior, Wis.
KATZ, Charles J., 1st Lieut., Oak Park, Ill.
LAWRENCE, Charles H., 1st Lieut., Chicago.
LEININGER, Alfred T., Captain, Rockford, Ill.
MILLER, Perry L., 1st Lieut., Adrian, Mich.
OLMSTED, Randolph F., Captain, Park Ridge, Ill.
POLLACK, Sampel, 1st Lieut., Chicago.
PUGSLEY, George W., 1st Lieut., Detroit.
PURVES, William L., 1st Lieut., Saginaw, Mich.
REGNER, Mathias F., 1st Lieut., Port Washington, Wis.
ROBINSON, LEON E., Captain, Aledo, Ill.
SARFATY, Isaac J., Captain, West Allis, Wis.
SCHIFF, Joseph H., 1st Lieut., Chicago.
SINAIKO, Russell P., 1st Lieut., Chicago.
SMITH, Edward C., 1st Lieut., Chicago.
SPECTOR, Israel H., 1st Lieut., Chicago.
SPRUNK, Carl J., 1st Lieut., Detroit.
STAMFLL, Benjamin B., 1st Lieut., Detroit.
SVERDLIN, Abe A., Captain, Milwaukee.
SWIONTKOWSKI, Stanley, Captain, Chicago.
THOMAS, Clyde O., Captain, Freeport, Ill.
WAGNER, Alphonse J., 1st Lieut., Brillion, Wis.
WATRY, Theodore D., 1st Lieut., Milwaukee.
WHITELEY, Robert K., 1st Lieut., Detroit.
VOLLMAR, George K., 1st Lieut., Detroit.
ZEMAN, Laddie W., 1st Lieut., Hinsdale, Ill.
ZIMMERMAN, Lazar E., Captain, Harvard, Ill.

EIGHTH CORPS AREA

The following medical reserve corps officers in the Eighth Corps Area, including the states of Texas, Colorado, Arizona and New Mexico, had been ordered to active duty by the Corps Area Commander up to November 8:

ADAMS, Blair S., 1st Lieut., Loveland, Colo.
AKERS, Elwyn N., 1st Lieut., Denver.
ALLAMON, Emmet, LaFayette, 1st Lieut., Sabine Pass, Texas.
ALLISON, Albert Murphy, 1st Lieut., Alice, Texas.
ALTHAUS, John William August, Captain, Fort Worth, Texas.
ANDERSON, William Douglas, Captain, Claremore, Okla.
ARNOLD, George Kenneth, Captain, Dallas, Texas.
BENNETT, John B., Captain, Lamesa, Texas.
BLAIR, James Robert Jr., 1st Lieut., Big Spring, Texas.
BLAKE, John V. Jr., 1st Lieut., Floresville, Texas.
BONNSTETTER, Harold John, 1st Lieut., Bandera, Texas.
BULLOCK, Bernard Eugene, 1st Lieut., Chnton, Okla.
CARTER, James Weldon, 1st Lieut., Palestine, Texas.
CATON, McKee, Captain, McAllen, Texas.
COMPERE, Clinton Lee, 1st Lieut., Decatur, Texas.
CONE, Frank, 1st Lieut., Houston, Texas.
COOPER, Elmer E., 1st Lieut., Nogales, Ariz.
COTTON, William Walker, 1st Lieut., Clinton, Okla.
CRADEN, Paul Joseph, 1st Lieut., El Reno, Okla.
CREEL, Gurley A., 1st Lieut., Kermit, Texas.
CULL, Herbert Graham, 1st Lieut., Houston, Texas.
DANDRIDGE, William Shelton, 1st Lieut., Dallas, Texas.
DAVENPORT, Harbert, Jr., 1st Lieut., Jacksonville, Texas.
DUDGEON, Howard Rush Jr., 1st Lieut., Waco, Texas.
FISHER, H. Calvin, 1st Lieut., Denver.
FLAMM, Kenneth R., 1st Lieut., Amarillo, Texas.
FOERSTER, Hervey A., Captain, Oklahoma City.
FRACHTMAN, Hirsh Julian, 1st Lieut., Houston, Texas.
FUNK, Gustavus D., 1st Lieut., El Reno, Okla.
GARRETT, Leslie Moyers, 1st Lieut., Corpus Christi, Texas.
GILLILAND, James O., 1st Lieut., Pampa, Texas.
GONZALEZ, Juan C. Jr., 1st Lieut., Benavides, Texas.
GOODLOE, Basil Lynn, 1st Lieut., El Paso, Texas.
GOODRUM, William A., 1st Lieut., Phoenix, Ariz.
GUICE, Leroy Edward, Captain, Sabinal, Texas.
HAHN, William B., 1st Lieut., Columbus, Texas.
HALPIN, Frank W., Captain, Fort Worth, Texas.
HART, Gaylord A., 1st Lieut., Dallas, Texas.
HEATLY, Maurice Dean, 1st Lieut., San Antonio, Texas.
HELLAMS, Alfred Allen, 1st Lieut., Dallas, Texas.

HENRY, Colvern Dewey, Captain, San Antonio, Texas.
HOWARD, Glenn T., 1st Lieut., Bruni, Texas.
HUBBARD, John Russell, 1st Lieut., Oklahoma City.
HUBBARD, Ralph W., Captain, Oklahoma City.
HUDSON, Granville W., 1st Lieut., San Antonio, Texas.
IVERS, William Maurice, 1st Lieut., Loveland, Colo.
JOHNSON, Homer B., 1st Lieut., Midland, Texas.
JONES, Thomas R., 1st Lieut., Beaumont, Texas.
JORDAN, Fred C. Jr., 1st Lieut., Phoenix, Ariz.
KAHLER, Glenn E., 1st Lieut., Buckholtz, Texas.
KNOLE, Ben E., 1st Lieut., Houston, Texas.
LAMBERSON, Harry Henry, 1st Lieut., Colorado Springs, Colo.
LANCASTER, G. M., 1st Lieut., Clovis, N. M.
LEGG, Eugene Pinsen, 1st Lieut., Dallas, Texas.
LIPAN, Edward M., 1st Lieut., Denver.
MARTIN, Howard C., 1st Lieut., Oklahoma City.
MARTIN, Scott Harrison, 1st Lieut., Hamilton, Texas.
MAXWELL, Ernest Arthur, 1st Lieut., San Antonio, Texas.
McCANN, Joseph William, 1st Lieut., Denver.
McCLOUD, Benjamin L. Jr., 1st Lieut., Graford, Texas.
McCONNELL, Jesse Maurice, 1st Lieut., Houston, Texas.
McGEE, Aubrey S., 1st Lieut., San Angelo, Texas.
MOURSUND, Walter H. Jr., Captain, Dallas, Texas.
NESTER, Charles R., 1st Lieut., Houston, Texas.
OLIVER, Thomas Mitchell, 1st Lieut., Waco, Texas.
ORR, Charles William, 1st Lieut., Houston, Texas.
PATERSON, Fred Lindley Jr., 1st Lieut., Mountain View, Okla.
PAUL, William G., 1st Lieut., Durant, Okla.
PAULSON, Alvin Winfred, Captain, Clinton, Okla.
PAWOL, Sylvester Edward, 1st Lieut., Clovis, N. M.
PAYNE, Ralph B., 1st Lieut., Amarillo, Texas.
PETICOLAS, John D., 1st Lieut., El Paso, Texas.
PHILLIPS, Claude Mason, 1st Lieut., Austin, Texas.
PORTER, George Leslie, Captain, Dallas, Texas.
POST, Samuel Perry, 1st Lieut., Boerne, Texas.
PRATT, Perry G., 1st Lieut., Denver.
REED, Emil Patrick, Captain, Brownsville, Texas.
RICHARDS, John Terrence, 1st Lieut., Rockdale, Texas.
ROBINSON, Harold L., Captain, Austin, Texas.
ROBISON, Edward W., 1st Lieut., Austin, Texas.
ROGERS, Galen Alonzo, Captain, Talihina, Okla.
RUCKER, John C. Captain, Dallas, Texas.
SALDIVAR, Julian Theodore, 1st Lieut., Austin, Texas.
SANFORD, Gilman E., 1st Lieut., Denver.
SCARBOROUGH, James S., Captain, Rusk, Texas.
SEASTRUNK, Oliver C., 1st Lieut., Franklin, Texas.
SHIVERS, George Clausman, Captain, Colorado Springs, Colo.

SPARKMAN, Robert Satterfield, 1st Lieut., Cincinnati.
STANLEY, John Frank, 1st Lieut., Yuma, Ariz.
STEEGER, Joseph Hamilton, 1st Lieut., Fort Worth, Texas.
STILES, Wendel A., Captain, Dallas, Texas.
STOKES, Robert C., Captain, Vernon, Texas.
STOUGH, AUSTIN R., 1st Lieut., McAlester, Okla.
THOMAS, Harold R., 1st Lieut., Austin, Texas.
TIGERTT, William D., 1st Lieut., Dallas, Texas.
TILDEN, James F., 1st Lieut., Olathe, Colo.
TUBBS, Harry Augustus, 1st Lieut., Temple, Texas.

TYLER, Monroe R., 1st Lieut., Eagle, Colo.
WALLACE, Gordon K., Captain, Dallas, Texas.
WEST, R. C., Captain, Hamilton, Texas.
WIERNIK, Harris, 1st Lieut., Lovelady, Texas.
WILSON, Harry G., 1st Lieut., Dallas, Texas.
WINBORN, Claude D., Captain, Dallas, Texas.
WINSHIP, Theodore O., 1st Lieut., Austin, Texas.
YARBROUGH, Cecil Gilbert Jr., 1st Lieut., Midland, Texas.
YATES, June, 1st Lieut., Grapevine, Texas.
ZINK, Linus Anthony, 1st Lieut., Pecos, Texas.

NINTH CORPS AREA

The following medical reserve corps officers of the Ninth Corps Area, which comprises the states of California, Oregon, Washington, Idaho, Montana, Wyoming, Utah and Nevada, had been ordered to active duty at the stations indicated by the Corps Area Commander, up to November 8:

ABRAMOPOULOS, Christos A., Major, San Francisco, 1st Military Area, Presidio of San Francisco.
ADAMS, Lewis N., 1st Lieut., Quinalt, Wash., 2d Military Area, Portland, Ore.
ADAMS, Morgan K., 1st Lieut., Sanitarium, Calif., Fort Lewis, Wash.
ARONSON, Samuel F., 1st Lieut., Seattle, Camp Murray, Wash.
AUTARD, Eugene J., 1st Lieut., San Francisco, Presidio of Monterey and Fort Ord, Calif.
BENSON, Seymour, 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
BERNSTEIN, Theodore I., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, California.
BIVINS, Thomas E., 1st Lieut., Fort Bragg, Calif., Presidio of Monterey and Fort Ord, Calif.
BOVENMYER, Earl S., 1st Lieut., Pocatello, Idaho, Presidio of Monterey and Fort Ord, Calif.
BRUCE, Robert A., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
BUMP, Robert I., 1st Lieut., Cheyenne, Wyo., Presidio of Monterey and Fort Ord, Calif.
CALCAGNO, Joseph S., 1st Lieut., San Jose, Calif., Presidio of Monterey and Fort Ord, Calif.
CHANDLER, Willard J., 1st Lieut., Woodburn, Ore., Vancouver Barracks, Wash.
CHAPMAN, Edwin S., 1st Lieut., San Fernando, Calif., Presidio of Monterey and Fort Ord, Calif.
CONOVER, George W. Jr., 1st Lieut., Wilbur, Wash., Fort Lewis, Wash.
CRALL, Herbert D., Lieut. Col., San Francisco, Surgeon's Office, Hq. Ninth Corps Area, Presidio of San Francisco.
DALE, Earl E., Major, Edgerton, Wyo., 3d Military Area, Salt Lake City.
DAVENPORT, Donald J., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
DURHAM, Milton W., 1st Lieut., La Grande, Ore., Fort Lewis, Wash.
EARL, Donald H., 1st Lieut., San Pedro, Calif., Fort MacArthur, Calif.
EDELSON, Zanly C., 1st Lieut., San Francisco, Presidio of San Francisco.
EVANS, Carvel S., Captain, Salt Lake City, 3d Military Area.
EVERETT, Ernest G., 1st Lieut., Ashland, Ore., Presidio of Monterey and Fort Ord, Calif.
FEUSNER, Henry D., 1st Lieut., Los Angeles, Fort Rosecrans, Calif.
FEY, Louis D., 1st Lieut., Seattle, Fort Lewis, Wash.
FRANZI, Antoini J., 1st Lieut., San Francisco, Presidio of San Francisco.
GARDNER, Elsworth L., 1st Lieut., Eugene, Ore., Fort McDowell, Calif.
GIANELLI, Virgil J., 1st Lieut., Stockton, Calif., Fort Scott, Calif.
GROSSBLAT, Jacob, 1st Lieut., Los Angeles, 1st Military Area, Presidio of San Francisco.
GUYETT, Harvey E., 1st Lieut., Idaho Falls, Idaho, Fort Lewis, Wash.
HAVERSTOCK, Richard T., 1st Lieut., Seattle, Fort Lewis, Wash.
HICKMAN, Harry S., 1st Lieut., Davenport, Wash., Fort Lewis, Wash.
HOLTZ, Paul Roscoe, Major, Lander, Wyo., 3d Military Area, Salt Lake City.
HORWITZ, Emanuel, Captain, Alcatraz Island, Calif., Fort McDowell, Calif.
HUNTINGTON, William H., Lieut. Col., Portland, Ore., Fort Lewis, Wash.

ISAAC, Ralph W., 1st Lieut., Pomeroy, Wash., Vancouver Barracks, Wash.
JACKEMY, Edward J., 1st Lieut., Oakland, Calif., Presidio of Monterey and Fort Ord, Calif.
JUMBLATT, Albert, Captain, Pacific Beach, Calif., Fort Rosecrans, Calif.
KINGSTON, George R., 1st Lieut., Wenatchee, Wash., Fort Lewis, Wash.
KONIGSBERG, Jerome, 1st Lieut., San Francisco, Presidio of Monterey and Fort Ord, Calif.
LARSON, Rudolph V., Captain, Smithfield, Utah, Fort Lewis, Wash.
LEE, George F., Captain, Union, Ore., Fort Stevens, Ore.
LEVAN, Norman E., 1st Lieut., Los Angeles, 1st Military Area, Presidio of San Francisco.
LIND, Laurie P., Major, Portland, Ore., 2d Military Area.
LLOYD, Robert E., 1st Lieut., San Francisco, Fort Lewis, Wash.
MAQUIRE, Joseph F., 1st Lieut., Ventura, Calif., Presidio of Monterey and Fort Ord, Calif.
McDONALD, Frank J., Captain, Bakersfield, Calif., Presidio of Monterey and Fort Ord, Calif.
MELLO, Henry G., 1st Lieut., Alameda, Calif., Presidio of Monterey and Fort Ord, Calif.
NELSON, Walfred A., 1st Lieut., Salt Lake City, Salt Lake City, Utah, Recruiting Officer.
NEWSON, Samuel J., Captain, Walla Walla, Wash., Fort Worden, Wash.
OHLMACHER, Joseph P., 1st Lieut., Missoula, Mont., Fort Lewis, Wash.
OSGOOD, Samuel B., 1st Lieut., Grants Pass, Ore., Presidio of Monterey and Fort Ord, Calif.
PEDERSEN, Christian B., Major, Tahoe, Calif., 1st Military Area.
QUALHEIM, Clarence B., Captain, Seattle, Fort Lewis, Wash.
RICH, David R., 1st Lieut., La Grande, Ore., Fort Lewis, Wash.
ROBBINS, Carl William, Lieut. Col., Eugene, Ore., Fort Lewis, Wash.
ROGERS, Thomas J., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
SAWYER, Malcolm H., 1st Lieut., North Twin Falls, Idaho, 3d Military Area.
SENER, Walter P., Captain, San Francisco, 1st Military Area.
SHAEFER, J. H., Lieut. Col., San Francisco, Surgeon's Office, Hq. Ninth Corps Area, Presidio of San Francisco.
SHARP, Paul W., 1st Lieut., Klamath Falls, Ore., Fort Lewis, Wash.
SHIER, Cyril W., Captain, Arcadia, Calif., Presidio of Monterey and Fort Ord, Calif.
SIRBU, Abraham B., 1st Lieut., San Francisco, Presidio of Monterey and Fort Ord, Calif.
SPRAGUE, Norman F., 1st Lieut., Beverly Hills, Calif., Presidio of Monterey and Fort Ord, Calif.
STRANQUIST, Henry C., Major, Ogden, Utah, 3d Military Area.
SZUKALSKI, Joseph P., 1st Lieut., Pasadena, Calif., 1st Military Area, Presidio of San Francisco.
TEN EYCK, Thomas G., Captain, Portland, Ore., Fort Lewis, Wash.
THOMAS, Leon B., Captain, Vancouver, Wash., Fort Lewis, Wash.
THOMPSON, Roger S., Captain, Seattle, Camp Murray, Wash.
TICHENOR, Ernest LaPoint, Captain, Fort Belknap, Harlem, Mont., 3d Military Area, Salt Lake City.
TOPPENBERG, David R., 1st Lieut., Loma Linda, Calif., Presidio of Monterey and Fort Ord, Calif.
VELONIS, Stamatis G., 1st Lieut., Nespelem, Wash., Fort Lewis, Wash.
VOGT, Paul R., 1st Lieut., The Dalles, Ore., Fort Lewis, Wash.
WHITAKER, Clifford W., Major, Tacoma, Wash., 2d Military Area, Portland, Ore.
WHITE, Alfred S., 1st Lieut., San Francisco, Presidio of Monterey and Fort Ord, Calif.
WOLF, Robert W., 1st Lieut., San Francisco, Presidio of San Francisco.
ZENER, Francis B., Major, Portland, Ore., Vancouver Barracks, Wash.

RESERVE PUBLIC HEALTH OFFICERS

The following physicians have taken their oaths as assistant surgeons in the reserve of the U. S. Public Health Service. Their home address and medical schools from which they graduated are indicated:

ALDRICH, Clarence K., New York, Northwestern University.
BEARDSLEY, Wayne P., Staten Island, N. Y., Jefferson Medical College.
BERKEBILE, Robert D., Cleveland, Ohio State University.
CARSTENSEN, Vincent H., New Orleans, State University of Iowa.
CRAWFORD, John G., Charlottesville, Va., University of Virginia.
FRAGIN, Irving D., New York, New York University.
FARBER, David N., Staten Island, N. Y., Ohio State University.
FORAKER, Alvan G., Pittsburgh, University of Pittsburgh.

GERSTEN, Samuel, Staten Island, N. Y., Syracuse University.
HANNON, Harland N., Louisville, Ky., Kansas City University.
JONES, Charles W., Baltimore, University of Maryland.
KING, William D. Jr., Miami, Ariz., Baylor University.
LUCAS, Paul W., Baltimore, Duke University.
MacKILLIP, Daniel, Jr., Cambridge, Mass., Tufts College Medical School.
MURPHY, C. Henry, Staten Island, N. Y., Georgetown University.
MYERS, Mark E., Charlottesville, Va., University of Virginia.
RAPPAORT, Eugene O., Staten Island, N. Y., University of Lausanne, Switzerland.
TRAIN, John B., New York, New York University.
VANDERHOOK, Ray H., Buffalo, College of Medical Evangelists.
WHITE, James N., Dallas, Texas, University of Texas.
WOLFE, Roy E., Denver, University of Colorado.

ORGANIZATION SECTION

EXHIBITS FOR MEDICAL SOCIETIES AND SCIENTIFIC ORGANIZATIONS

Exhibits pertaining to the work of the various departments of the American Medical Association and to subjects in which those departments are interested have been prepared for medical societies and other scientific organizations.

The exhibits are available on a loan basis. Responsibility for installation and demonstration of the exhibits ordinarily must be borne by the organization to which the material is lent. Except in special instances, the American Medical Association will be unable to send its own personnel for such duties.

Requests for material should be instituted as far in advance as possible, so that the proper reservations can be made. Exact shipping addresses and dates should be given when the request is made.

Further information may be obtained from
Director, Scientific Exhibit, American Medical Association,
535 North Dearborn Street, Chicago.

13. Medical Discoveries of a Century.

An exhibit, originally shown at A Century of Progress Exposition in Chicago, consisting of nine groups of figures—Beaumont, Morton, Pasteur, Lister, Roentgen, Theobald Smith, Curie, Ehrlich and Banting. Each group is set in a case with indirect lighting. Models are made of plaster and require great care in handling.

Space required, an area 10 feet wide by 6 feet deep (or 16 linear feet); no background necessary.

Electrical connections, nine outlets, each for a 60 watt lamp.
Shipping weight, 672 pounds.

16. Heroes of Medicine.

An exhibit, originally shown at the Golden Gate International Exposition in San Francisco, consisting of ten groups of figures—McDowell, Beaumont, Long, Holmes, Sims, Welch, Gorgas, Theobald Smith, Ricketts and Reed. Each group is set in a case with indirect lighting. Models are made of rubber and are quite substantial.

Space required, area 10 feet wide by 10 feet deep (or 21 linear feet).

Electrical connections, ten outlets using a total of 400 watts.
Shipping weight, 840 pounds.

30. Hospital Service in the United States.

An exhibit from the Council on Medical Education and Hospitals presenting data on hospitals collected in the annual survey; miscellaneous posters and pamphlets.

Space required, one or two booths according to material selected, together with tables for literature.

Shipping weight, according to material selected.

32. Medical Education in the United States.

An exhibit from the Council on Medical Education and Hospitals consisting of charts showing statistics on medical education in the United States, together with miscellaneous maps and literature.

Space required and shipping weight, according to amount of material selected.

34. Tularemia (spread and control).

An exhibit from the Scientific Exhibit of the American Medical Association made in conjunction with Dr. Walter M. Simpson, Miami Valley Hospital, Dayton, Ohio, and Dr. Edward Francis, U. S. Public Health Service, Washington, D. C., consisting of transparencies showing clinical cases of tularemia and posters on panels showing the prevalence, animal

hosts, insect vectors and what to do to prevent infection. An exposition "microscope" shows the tularemia organism.

Space required, an area 10 feet wide by 6 feet deep; no background necessary.

Electrical connections, two outlets for lamps in transparency case and exposition "microscope" using 255 watts.

Shipping weight, 297 pounds.

35. Tularemia (pathology).

An exhibit from the Scientific Exhibit of the American Medical Association of photographs, photomicrographs and roentgenograms collected by Dr. Walter M. Simpson and Dr. Edward Francis, showing the pathologic changes of tularemia in animals and man.

Space required, an area 10 feet wide by 6 feet deep; no background necessary.

Electrical connections, one outlet for lamps in transparency case using 240 watts.

Shipping weight, 260 pounds.

50. Use and Abuse of Barbiturates.

An exhibit from the Council on Pharmacy and Chemistry consisting of posters showing the use and abuse of the barbiturates; a chart giving the names and chemical formulas of thirty products on the market; an exposition file and New and Nonofficial Remedies giving additional information.

Space required, a booth with back wall 10 feet wide and side walls 6 feet deep on which to hang charts and posters; a table for exposition file and N. N. R.

Shipping weight, 103 pounds.

51. Work of the Council on Pharmacy and Chemistry.

An exhibit from the Council on Pharmacy and Chemistry consisting of miscellaneous posters, each 22 by 28 inches, from which selections can be made to fit any space desired.

Shipping weight, from 40 to 50 pounds.

52. Work of the A. M. A. Chemical Laboratory.

An exhibit from the Chemical Laboratory, similar to the one from the Council on Pharmacy and Chemistry, consisting of posters from which selections can be made to fit any space desired.

Shipping weight, from 40 to 50 pounds.

53. Work of the Council on Foods and Nutrition.

An exhibit from the Council on Foods and Nutrition consisting of miscellaneous posters, each 22 by 28 inches, containing the various items of information concerning the work of the Council.

Shipping weight, according to amount of material selected.

54. Work of the Council on Physical Therapy.

An exhibit from the Council on Physical Therapy consisting of miscellaneous charts in frames, each 22 by 28 inches, together with selected apparatus. The following groups have been found of interest: short wave diathermy; simple apparatus for physical therapy; miscellaneous posters dealing with the work of the Council.

Space required, variable according to kind of material selected.

Electrical connections, one or more outlets if mechanical material is selected.

Shipping weight, variable according to material selected.

55. Posture.

An exhibit from the Council on Physical Therapy consisting of a manikin for visitor participation showing correct and incorrect posture; transparencies showing reasons for good

posture and panels with posters showing the relation of sitting and posture, the feet and posture, the causes of poor posture and recommendations for good posture. An exposition file gives additional information.

Space required, an area 10 feet wide by 6 feet deep; no background necessary; two small tables, one for manikin and one for exposition file.

Electrical connections, three outlets for lamps in cases using a total of 440 watts.

Shipping weight, 368 pounds.

61. Medical Economics.

An exhibit from the Bureau of Medical Economics consisting of miscellaneous charts; a rack for literature showing the publications of the Bureau and two exposition files containing various items of information concerning medical economics.

Space required, a booth with back wall 10 feet wide and two side walls each 6 feet deep.

Shipping weight, 240 pounds.

63. Industrial Health.

An exhibit from the Council on Industrial Health consisting of a group of posters showing the status of industrial health in the United States together with an exposition file giving additional information.

Space required, a booth with back wall 10 feet wide and side walls on which to hang posters; table for exposition file.

Shipping weight, 166 pounds.

64. Silicosis and Pneumoconiosis.

An exhibit from the Council on Industrial Health in conjunction with the Saranac Laboratory consisting of transparencies and panels showing the essential facts about benign pneumoconiosis, simple nodular silicosis, simple conglomerate silicosis, tuberculosilicosis and asbestosis.

Space required, an area 30 feet wide by 6 feet deep; no background necessary.

Electrical requirements, five outlets for transparencies, alternating current, 400 watts.

Shipping weight, 991 pounds.

66. Basic Science Laws.

An exhibit from the Bureau of Legal Medicine and Legislation consisting of six charts and frames, each 22 by 28 inches, together with a shadow box.

Space required, a booth with back wall 10 feet wide, and side walls 6 feet deep (15 linear feet).

Electrical connections, one outlet, 120 watts.

Shipping weight, 154 pounds.

67. Medical Legislation and Medicolegal Topics.

An exhibit from the Bureau of Legal Medicine and Legislation consisting of miscellaneous charts in frames, each 22 by 28 inches.

Space required, a booth with back wall 10 feet wide and side walls 6 feet deep (or 15 linear feet).

Shipping weight, 60 pounds.

70. Cutaneous Manifestations of Tuberculosis.

An exhibit from the Scientific Exhibit of the American Medical Association, in conjunction with the Section on Dermatology and Syphilology, consisting of four panels each 5 feet high and 3 feet wide, showing photographs of cutaneous tuberculosis and conditions which simulate it.

Space required, an area 10 feet wide by 3 feet deep; no background necessary.

Shipping weight, 166 pounds.

71. Cutaneous Granulomas.

An exhibit from the Scientific Exhibit of the American Medical Association, in conjunction with the Section on Dermatology and Syphilology, consisting of photographs of various granulomas (other than tuberculosis and syphilis), including one panel of leprosy and one panel of drugs. The photographs are mounted on six panels, each 5 feet high and 3 feet wide, with legs $2\frac{1}{2}$ feet high, which can be installed readily.

Space required, an area 12 feet wide by 3 feet deep; no background necessary.

Shipping weight, 250 pounds.

72. Cutaneous Manifestations of Syphilis.

An exhibit from the Scientific Exhibit of the American Medical Association, in conjunction with the Section on Dermatology and Syphilology, consisting of about 150 photographs of the various syphilitic lesions in different stages of the disease. The photographs are mounted on panels 5 feet high by 3 feet wide, with legs $2\frac{1}{2}$ feet high, which can be installed readily.

Space required, an area 18 feet wide by 3 feet deep; no background necessary.

Shipping weight, 327 pounds.

78. Aesculapius, Hygeia, Hippocrates and Osler.

Four plaster plaques in bas-relief from the Bureau of Exhibits showing Aesculapius, Hygeia, Hippocrates and Osler. Each figure is $8\frac{1}{2}$ feet high, 3 feet wide and 6 inches thick. Because of the fragile nature of the plaques, they will be sent only where they can be suitably installed.

Shipping weight: Aesculapius, 343 pounds; Hygeia, 354 pounds; Hippocrates, 300 pounds, and Osler, 366 pounds.

82. Treatment of Early Syphilis.

An exhibit prepared in conjunction with the United States Public Health Service consisting of ten posters, each 22 by 28 inches, together with an exposition file containing various items of information about the treatment of early syphilis. (A duplicate of this exhibit can be obtained also from the United States Public Health Service, Washington, D. C.)

Space required, a booth with back wall 10 feet wide and side walls 6 feet deep.

Shipping weight, 125 pounds.

84. Treatment of Prenatal Syphilis.

An exhibit prepared in conjunction with the United States Public Health Service, consisting of ten posters, each 22 by 28 inches, together with an exposition file containing various items of information about the treatment of prenatal syphilis. (A duplicate of this exhibit can be obtained also from the United States Public Health Service, Washington, D. C.)

Space required, a booth with back wall 10 feet wide and side walls 6 feet deep.

Shipping weight, 81 pounds.

86. Treatment of Late and Latent Syphilis.

An exhibit prepared in conjunction with the United States Public Health Service, consisting of ten posters, each 22 by 28 inches, together with an exposition file containing various items of information about the treatment of late and latent syphilis. (A duplicate of this exhibit can be obtained also from the United States Public Health Service, Washington, D. C.)

Space required, a booth with back wall 10 feet wide and side walls 6 feet deep.

Shipping weight, 119 pounds.

91. Hygeia in Office, School and Home.

An exhibit prepared in conjunction with *Hygeia*, the Health Magazine, consisting of five dioramas showing the use of *Hygeia* in office, school and home.

Space required, an area 10 feet wide by 3 feet deep; no background necessary.

Electrical connections, five outlets, requiring a total of 300 watts.

Shipping weight, 250 pounds.

95. Anesthesia.

An exhibit from the Scientific Exhibit of the American Medical Association, consisting of charts, transparencies and an exposition file giving information concerning anesthesia.

Space required, a booth with back wall 10 feet wide and side walls 6 feet deep.

Electrical requirements, one outlet using 240 watts.

Shipping weight, 267 pounds.

OFFICIAL NOTES

THIRD ANNUAL CONGRESS ON INDUSTRIAL HEALTH

Arrangements have been completed for the third annual Congress on Industrial Health sponsored by the American Medical Association, which will be held Monday and Tuesday, Jan. 13 and 14, 1941, at the Palmer House in Chicago.

These meetings are open to all physicians and others interested in the industrial health movement. There is no registration fee. Topics and speakers are as follows:

OPENING SESSION, MONDAY, 9:45 A. M.

Report of the Council on Industrial Health.

STANLEY J. SEEGER, M.D., Chairman, Milwaukee.

The Physician in Industry and National Defense.

IRVIN ABELL, M.D., Chairman, Health and Medical Committee in the Council of National Defense, Louisville, Ky.

Current Needs in Industrial Hygiene Research.

PHILIP DRINKER, Professor of Industrial Hygiene, Harvard University, Boston.

The Special Nature of Industrial Practice.

C. O. SAPPINGTON, M.D., Chicago.

Disability Evaluation in Silicosis.

J. L. BLAISDELL, M.D., Porcupine Clinic for Silicosis Research, St. Mary's Hospital, Timmins, Ontario.

Red Lacquer Room

MONDAY, 2 P. M.

HAND INJURIES

Anatomic Diagnosis of Injuries of the Hand.

JAMES M. WINFIELD, M.D., Associate Professor of Surgery, Wayne University College of Medicine, Detroit.

Treatment of Superficial Hand Injuries and Burns.

HARVEY S. ALLEN, M.D., Chicago.

Division of the Nerves and Tendons of the Hand.

MICHAEL MASON, M.D., Chicago.

Importance of Purposeful Splinting Following Injuries of the Hand.

HENRY C. MARBLE, M.D., Boston.

Prevention and Treatment of Hand Infections.

SUMNER L. KOCH, M.D., Chicago.

Red Lacquer Room

MONDAY, 2:30 P. M.

AVAILABILITY OF TRAINED INDUSTRIAL HEALTH PERSONNEL

The Trained Industrial Nurse.

RUTH HOULTON, R.N., Secretary, Industrial Nursing Section, National Organization for Public Health Nursing, New York.

The Industrial Hygiene Engineer.

(Speaker to be announced.)

The Safety Engineer.

W. H. CAMERON, Managing Director, National Safety Council, Inc., Chicago.

The Medical Industrial Hygienist.

PAUL A. NEAL, M.D., Chief of the Division of Industrial Hygiene, National Institute of Health, U. S. Public Health Service, Bethesda, Md.

The Physician in Industry.

ROBERT T. LEGGE, M.D., University of California, Berkeley, Calif.

Room 8

MONDAY, 6:30 P. M.

An informal dinner and round table discussion intended primarily for state and county medical society committees on industrial health will be held. The subject matter for discussion will include problems of organization and plans for future activity.

TUESDAY, 9:30 A. M.

Employment of the Physically Handicapped.

D. L. LYNCH, M.D., President, American Association of Industrial Physicians and Surgeons, Boston.

Aging as a Problem of Industrial Health.

EDWARD J. STIEGLITZ, M.D., Research Associate in Gerontology, National Institute of Health, U. S. Public Health Service, Bethesda, Md.

ACUTE RESPIRATORY DISEASE IN INDUSTRY

Incidence and Costs of Acute Respiratory Disease in Industry.

ANTHONY J. LANZA, M.D., Assistant Medical Director, Metropolitan Life Insurance Company, New York.

Respiratory Disease and Air Conditioning.

CAREY P. McCORD, M.D., Chairman, Committee on Air Conditioning of the American Medical Association, Detroit.

The Role of the Physician in Industry in the Control of Acute Respiratory Disease.

GEORGE M. PIERSOL, M.D., Philadelphia.

Red Lacquer Room

TUESDAY, 2 P. M.

INDUSTRIAL OPHTHALMOLOGY

Economic Importance of Visual Disability in Industry.

LEONARD GREENBURG, M.D., Chairman, Industrial Advisory Committee of the National Society for the Prevention of Blindness, New York.

Essentials of First Aid and Later Management of Industrial Eye Injuries.

SIDNEY WALKER JR., M.D., Chicago.

Detection and Control of Defective Vision in Industry.

ARTHUR M. CULLER, M.D., Dayton, Ohio.

Protective Equipment for Eyes in Industry.

THOMAS D. ALLEN, M.D., Associate Clinical Professor of Ophthalmology at Rush Medical College, Chicago.

HENRY F. CARMAN, M.D., San Francisco.

Red Lacquer Room

WEDNESDAY, JANUARY 15

On the day following the congress, the Chicago Medical Society will conduct clinics illustrating practical problems in industrial medicine, industrial hygiene and traumatic surgery.

On the same day the Chicago Medical Society will hold a dinner and evening meeting on the relationship of the private practitioner to the industrial health movement. The program will be:

Industrial Health—A Medical Opportunity.

STANLEY J. SEEGER, M.D., Chairman, Council on Industrial Health, American Medical Association, Milwaukee.

Medical Service for the Small Plant.

ANTHONY J. LANZA, M.D., New York.

The Control of Syphilis in Industry.

HAROLD A. VONACHEN, M.D., Peoria, Ill.

Further details regarding clinics and other demonstrations will be provided registrants at the congress, all of whom are invited to participate.

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the annual session at Cleveland on June 3, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the programs, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in THE JOURNAL and monthly in Hygieia, the Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

November 27. Through Hospital Corridors.

December 4. Paging Doctor Drew.

December 11. The Family's First Friend.

WOMAN'S AUXILIARY

Kansas

Members of the Montgomery County Medical Society and their wives met at the country club at Cherryvale, September 29, for a picnic supper. While the doctors enjoyed golf and target shooting the wives enthusiastically decided to become active in auxiliary work. Dr. and Mrs. Charles Miller were guests, and Mrs. Miller, who is councilor of the third district, presented objectives of the auxiliary today. Dr. and Mrs. T. D. Blasdel of Parsons were also guests, and Mrs. Blasdel, president of the auxiliary to the state society, suggested plans for the year. Mrs. H. O. Bullock of Independence was elected president and a meeting date was set at which time other officers will be elected and committees appointed.

Mississippi

The doctors' wives of Monroe County entertained the visiting auxiliary members of the Northeast Mississippi Thirteen Counties' Medical Society, September 10, at the home of Mrs. W. N. Reed. Mrs. Bernard Patrick, the president, introduced the speaker, Dr. Augustus Street, of Vicksburg, president-elect of the Mississippi State Medical Association. Mrs. Augustus Street urged the auxiliary's liberal offering for the Preventorium Fund. Mrs. Stanley Hill, of Corinth, gave a paper on "Animal Experimentation."

Members of the Adams County auxiliary and their husbands were entertained, October 2, at the home of Dr. and Mrs. W. K. Stowers, Natchez. Dr. E. E. Benoist, master of ceremonies, presented Dr. W. H. Anderson, Boonerville, president of the Mississippi State Medical Association, and Mrs. E. C. Parker, Gulfport, president of the woman's auxiliary to the state medical association. Dr. Anderson urged the wives to study ways of helping improve the service their husbands offer, to welcome opportunities of imparting information to the laity and thus strengthen confidence in the profession, and to strive to be the leaders in work related to medicine.

The officers of the state auxiliary met, October 3, with Mrs. Henry Boswell at the preventorium. The group voted \$30 a month to keep two children at the preventorium.

Nebraska

The auxiliary to the Lancaster County Medical Society met, October 7, at the home of Mrs. Floyd Rogers of Lincoln. Prof. O. H. Binson, of Lincoln High School, talked on his experiences as a member of the Educational Policies Commission and the American Youth Commission.

The auxiliary to the Omaha-Douglas Counties Medical Society held a Harvest Home Benefit Dinner, October 9, at the summer residence of Dr. and Mrs. C. C. Tomlinson. Proceeds from the dinner will benefit the projects adopted at the recent Membership Tea; namely, a subscription to *Hygeia* to all 102 of Omaha's public and parochial schools, the Community Chest, the School Free Lunch Fund and the Nebraska Tuberculosis Health Camp.

A joint dinner meeting of the tri-county auxiliary No. 1 and the Tri-County Medical Society was held, September 26, at the St. Francis Hospital in Grand Island. Mrs. Elmer Hansen, Lincoln, spoke on auxiliary problems; Mrs. J. G. Woodin, president of the auxiliary, talked on "A Look Ahead." Mrs. A. D. Brown, Central City, state president, addressed the group.

Oregon

The woman's auxiliary to the Oregon State Medical Society held its fourteenth annual meeting, September 5, at Eugene with seventy members in attendance. Mrs. V. E. Holcombe, president of the woman's auxiliary to the American Medical Association, was guest of honor. Dr. Hans Lisser, clinical professor of medicine at the University of California Medical School, spoke on "Hypothyroidism," with colored motion picture demonstrations.

Officers for the coming year were installed at the closing session: Mrs. Charles Edwin Sears, Portland, president; Mrs. Charles Hunt, Eugene, president-elect; Mrs. Merle Taylor,

Portland, corresponding secretary; Mrs. Laurence Serrurier, Portland, recording secretary, and Mrs. Paul Lind, Portland, treasurer.

Mrs. Holcombe attended the board meeting of the auxiliary to the Multnomah County Medical Society, September 9, and was guest of honor at a luncheon held at the Town Club. Twenty-six members attended. The auxiliary began its fall activities with a meeting, September 23, at the Portland Golf Club, with forty members present. This is a social occasion each year with bridge and visiting after luncheon.

Six volunteers from the auxiliary assisted with the annual open house and tea, October 5, at the Louise Home for Girls, a charitable organization. Members also assisted with the Silver Tea at Doernbecker Hospital for crippled children, September 21. The auxiliary to the Coos-Curry Counties Medical Society reports that at its first meeting in September the members worked on garments for the county poor farm.

Pennsylvania

The auxiliary honored its medical advisers at luncheon and heard an important lecture on "The World to Come" by Maurice Hindus, a journalist. Entertainment comprised a bus trip to Atlantic City for guests, music and talks by prominent speakers.

The annual meeting of the woman's auxiliary to the Medical Society of the State of Pennsylvania met in Philadelphia with more than 400 members in attendance. Mrs. V. E. Holcombe, president of the national auxiliary, was a guest. From the reports of the committees, it was found that during the current auxiliary year over \$5,500 had been contributed to the Benevolence Fund, Pennsylvania's own plan for caring for needy medical men and their families, contributed to by county groups each year. The auxiliary has contributed over \$37,000 to the fund in the past ten years. Pennsylvania, while not holding its place in national *Hygeia* sales, still did considerable work in that field. The state has followed the program of the national auxiliary and has reached over 5,000 in lay groups with public relation programs. The state auxiliary has a balance of over \$1,600 this year after all bills have been met. The history of the work of the state auxiliary in book form being made by the archives chairman is nearly completed. Twenty counties had model exhibits of original design showing their work in their home fields.

The woman's auxiliary to the Philadelphia County Medical Society began the season with the meeting of the state medical society in Philadelphia, followed by a meeting, October 8. Dr. Edward L. Bortz, president, Philadelphia County Medical Society, regards the work of organized medicine as a function of the auxiliary. He offered to provide physicians to report on the affairs of the county and suggested the ways and means by which the auxiliary might be most helpful. The health education chairman, Mrs. M. Fraser Percival, is ready to place speakers from the bureau of the Philadelphia County Medical Society before clubs.

South Carolina

Mrs. Charles P. Corn, president of the auxiliary to the Southern Medical Association, spoke at the September meeting of the auxiliary to the Greenville County Medical Society. She reported that members in Virginia and North Carolina have endowed beds for tuberculous patients in two sanatoriums. They are memorial beds in which members of doctors' families are given preference. In Alabama the auxiliary maintains a student loan fund.

The auxiliary to the Oconee County Medical Society recently purchased for the library of the Oconee County Hospital an aid for doctors who wish to find references in the medical books placed in the library by the Oconee County Medical Society. Guest speaker at the recent meeting was Dr. E. A. Hines, secretary of the South Carolina Medical Association.

The Spartanburg county medical auxiliary met recently, with Mrs. Charles P. Corn of Greenville, president of the Woman's Auxiliary to the Southern Medical Association, as guest speaker. Another guest was Dr. Ruth Frank Pugh of Converse College.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Personal.—Dr. Hugh F. Dormody, Monterey, was recently elected governor of district 106 of the Rotary International. —Dr. Lee A. Stone, Madera, was elected president of the health officers' department of the League of California Cities at a meeting, September 18, in San Diego.

Program for Pertussis Immunization Proposed.—The San Francisco Department of Health is planning to establish an immunization program against pertussis in a baby welfare center located in a section of the city where economic conditions generally prohibit a given family from securing this service from its private physician. After a trial period the program may be extended to other centers operated by the department if conditions show a need for the service and the experience of the trial station justifies its expansion. While no funds are now available in the present fiscal budget, it is hoped that a sufficient amount will be obtained to launch this work. It was pointed out that the cost of the material alone to the department for one pertussis immunization is eight times the cost of the material used for a complete immunization against diphtheria. The change was planned after the present policy of the department with respect to pertussis immunization was reviewed. Before a decision was made, opinions were requested from some pediatricians in the city and professors in this specialty at the medical schools of Stanford and California universities.

FLORIDA

Fraudulent Licenses Appear.—Two licenses recorded with the state board of medical examiners were recently declared fraudulent and are, according to the board, indications that the diploma mill racket is again being revived. One license, recorded by Lyle Park Johnson last April, was purportedly issued by the old Eclectic Board of Medical Examiners in 1919. Until recently Johnson had been practicing as a naturopath. The other license was recorded in Munroe County in September 1939 by Gavilla Lopez and was also an eclectic license purportedly issued in 1919. Lopez had also been practicing as a naturopath in Tampa. Both men possessed diplomas from the Baltimore Eclectic Medical College, the state medical board reported.

ILLINOIS

Society News.—Dr. Harold C. Lueth, Evanston, discussed "Management of Bright's Disease with Special Reference to the Acute Stage" before the Adams County Medical Society in Quincy, October 14. —Dr. George K. Fenn, Chicago, addressed the Madison County Medical Society in Granite City, November 1, on congestive heart failure. —Dr. Walter C. Alvarez, Rochester, Minn., discussed "Functional Gastrointestinal Disorders" before the Peoria Medical Society, November 12. —The Tri-County Medical Society, comprising Warren, Knox and Henry counties, met in Monmouth, November 1, with the following speakers: Drs. Charles E. Galloway, Evanston, on "Diseases of the Cervix and Treatment"; Chauncey C. Maher, "Treatment of Cardiac Edema"; Philip Lewin, "Infantile Paralysis," and Morris Fishbein, Editor of THE JOURNAL, "The Medical Profession Prepares." All are of Chicago. —Dr. Wayne W. Fox, Evanston, addressed the Christian County Medical Society at Taylorville, October 30, on pneumonia. —Dr. Richard S. Weiss, St. Louis, discussed "Precancerous Lesions of the Skin" before the St. Clair County Medical Society in Belleville, November 6. —Dr. Paul A. Campbell, Chicago, discussed "Medical Problems of Combat Aviation" before the La Salle County Medical Society, October 24, at Starved Rock State Park.

Chicago

Winners of Child Research Grant.—The Institute of Medicine of Chicago announces that the Elizabeth McCormick Child Research Grant of \$1,500 for 1940-1941 has been divided among Drs. Mila I. Pierce, Evanston, Clayton J. Lundy and Heyworth N. Sanford for the continuation of the investigations begun under their 1939-1940 grants. Dr. Lundy's sub-

ject is heart sound records in rheumatic heart disease; Dr. Pierce's, leukosis, and Dr. Sanford's, role of qualitative platelet factors in the coagulation of the blood.

Symposium on the Adult Offender.—The Chicago Academy of Criminology and the Chicago Society for Personality Study held a joint meeting, October 30. The theme of the session was "The Adult Offender." The speakers included:

Dr. Marvin Sukov, psychiatrist, division of the criminologist, State of Illinois, Personality Study of the Adult Offender.
Hans Riemer, supervisor of education, Indiana State Penitentiary, Practical Application in a Prison Program.
Samuel Daykin, sociologist, division of pardons and paroles, State of Illinois, Practical Application in Probation, Parole and Social Readjustments.

Harry M. Fisher, judge of Cook County Circuit Court, and Ernst W. Puttkammer, professor of law, University of Chicago, discussed the presentations.

INDIANA

Society News.—Dr. Jay Arthur Myers, Minneapolis, discussed "The Control of Tuberculosis" before the Fort Wayne Medical Society in Fort Wayne, October 15. —The Delaware-Blackford County Medical Society was addressed in Muncie, October 15, by Drs. Joseph C. Silvers and Nila G. K. Covalt, Muncie, on "Organotherapy of Menstrual Irregularities" and "Organotherapy of the Menopause" respectively. —Dr. Daniel L. Sexton, St. Louis, addressed the Gibson County Medical Society in Princeton, October 14, on "Endocrine Treatment in General Practice." —Dr. Eugene L. Bulson, Fort Wayne, discussed "The Symptoms and Diagnosis of Foreign Bodies in the Air and Food Passages" before the Fort Wayne Academy of Medicine and Surgery, November 12. The academy was addressed, November 19, by Dr. Grover C. Penberthy, Detroit, on "The Surgical Management of Appendicitis."

KANSAS

Changes in Health Officers.—Dr. Hugh M. Swaney, Goodland, has been named health officer of Sherman County. Dr. Charles A. Dieter, Harper, has been appointed in charge of Harper County to succeed the late Dr. Clarence E. Ressler, Anthony, and Dr. James N. Hill, Hutchinson, health officer of Reno County.

Society News.—The Shawnee County Medical Society was addressed, November 4, by Dr. Andrew W. McAlester III, Kansas City, Mo., on "Practical Ophthalmic Therapy." —Dr. Henry M. Winans, Dallas, Texas, discussed "Anemia—Diagnosis of Difficult Cases" before the Wyandotte County Medical Society, November 5, in Kansas City. The society was addressed, October 15, by Drs. Albert J. Rettenmaier on "Biliary Stones with Emphasis on the Exploration of the Common Duct" and Harold V. Holter, "Sterility."

MASSACHUSETTS

Petition Supports Contraceptive Advice.—The Committee for the Defense of Medical Rights has issued a statement in support of an initiative petition to amend the Massachusetts laws relating to prevention of pregnancy. The change in the law would allow physicians to provide medical contraceptive information and care to married persons for the protection of life or health. The petition asks the legislature to amend sections 20 and 21 of chapter 272 of the general laws by adding at the end thereof the following:

The provisions of this section and of section twenty which relate to the prevention of pregnancy and the prevention of conception shall not apply to treatment or prescription given to married persons for protection of life or health by or under the direction of physicians registered in accordance with the provisions of Chapter 112; nor to teaching in chartered medical schools; nor to publication or sale of medical treatises or journals.

The statement issued by the Committee for the Defense of Medical Rights reads:

The initiative petition proposed is for a bill to insure to physicians the right to protect the life, health, and reason of married persons when these might be endangered by pregnancy. It is designed to prevent the legal interference with this phase of the practice of medicine, which has only recently resulted from the enforcement of an old Massachusetts statute.

The principle of legal freedom for physicians to provide contraceptive medical care to married persons whose physical or mental condition would suffer by pregnancy or who could be expected to produce only seriously defective individuals, has been approved by the American Medical Association, and by many other medical and religious bodies.

Support of this petition does not imply support of either the methods or philosophy of "birth control." It means only support of the principle of freedom in the licensed teaching and practice of medicine.

The initiative petition is so designed as to protect morality and marital security and to bring under licensed control the present, widespread bootleg traffic in contraceptive information and material, which we deplore.

Physicians who wish to aid in obtaining signatures to the initiative petition may obtain blanks by getting in touch with Somers H. Sturgis, secretary of the Committee for the Defense of Medical Rights, 270 Commonwealth Avenue, Boston.

NEW YORK

Society News.—Willard H. Wright, Ph.D., Washington, D. C., addressed the Buffalo Academy of Medicine, October 30, on "Common Parasitic Infestations in Children." Dr. Jacob Arnold Bargen, Rochester, Minn., addressed the section of surgery, November 6, on "Differentiation Between Various Types of Ulcerative Colitis and Their Management."—Dr. Harry Dan Vickers, Little Falls, addressed the Herkimer County Medical Society, October 8, on "Surgical Aspects of a Major Railroad Accident."—Dr. William P. van Wagenen, Rochester, addressed the Jefferson County Medical Society, October 10, on "Head Injuries."—Clarence Cook Little, Sc.D., Bar Harbor, Maine, and Dr. William P. Healy, New York, addressed the Medical Society of the County of Nassau, Garden City, October 29, on "Recent Advances in Cancer Research" and "Cancer of the Female Pelvis" respectively.

New York City

Second Harvey Lecture.—Dr. Charles H. Best, Toronto, Canada, will deliver the second Harvey Society Lecture of the current series at the New York Academy of Medicine, November 28. Dr. Best's subject will be "Thrombosis and the Action of Heparin."

Lecture by Dr. Corner.—Dr. George W. Corner, director of the department of embryology of the Carnegie Institution of Washington, located in Baltimore, will deliver a lecture at Cornell University Medical College, December 10, under the auspices of the Nu Sigma Nu Fraternity. Dr. Corner's subject will be "The Ovarian Cycle of the Rhesus Monkey."

OHIO

Personal.—Dr. Joseph J. Kotershall, Cleveland, was recently honored at a surprise dinner given by about seventy-five physicians. It was said that the dinner was in appreciation of "the guiding hand he has always offered to youngsters in the profession." The group gave him a watch as a memento.

University News.—The General Education Fund has recently added \$12,700 to the grant previously made to the Brush Foundation, Western Reserve University School of Medicine, Cleveland, for the study of child health and development under the direction of William Walter Greulich, Ph.D., director of the foundation.

Postgraduate Lectures.—The autumn postgraduate series of lectures sponsored by the Mahoning County Medical Society were presented in Youngstown, November 14-15, with Dr. Henry L. Bockus, Philadelphia, as the speaker. His subjects were "Present Clinical Status of Chronic Gastritis," "What Constitutes Adequate Therapy for Chronic Peptic Ulcer," "Practical Application of Recent Advances in Our Knowledge of Liver Functions," "Diagnosis and Management of Chronic Ileitis and Ileocolitis" and "Diagnosis and Management of the Irritable Colon."

PENNSYLVANIA

Postgraduate Assembly.—The Harrisburg Academy of Medicine presented its annual Postgraduate Assembly, November 14, with the following speakers:

Dr. J. C. Wetherall, Syracuse, N. Y., The Nodular Goiter—Its

Dr. J. C. Wetherall, Syracuse, N. Y., The Nodular Goiter—Its

Dr. Chevalier L. Jackson, Philadelphia, Broncho-Esophagology in Relation to General Medicine.

Dr. Temple S. Fay, Philadelphia, Further Observations on Refrigeration in Human Beings.

Philadelphia

Personal.—Dr. Frederick C. Smith has been elected editor of the *Weekly Roster and Medical Digest*, official organ of the Philadelphia County Medical Society, to succeed the late Dr. Samuel Horton Brown.

Joint Orthopedic Meeting.—The section of orthopedic surgery of the New York Academy of Medicine and the orthopedic section of the Philadelphia County Medical Society held a joint meeting at Jefferson Medical College, November 15. The speakers included:

Dr. James R. Martin, A Simplified Apparatus for Use After Surgery for Torticollis.

Dr. Arthur Bruce Gill, Early Changes in Legg-Perthes' Disease and the Cyclic Course It Pursues.

Dr. Oscar V. Batson, The Vertebral Venous System.

Drs. Ernest A. Bray and Henry I. Sigmund, Injection Treatment for Low Back and Sciatic Pain.

Drs. Benjamin Franklin Buzby and Allan D. Wallis, Spine Fusion—A Modified Hibbs Technic.

RHODE ISLAND

Society News.—At a meeting of the Providence Medical Association, October 7, Drs. Halsey DeWolf, chairman of the state board on medical preparedness, and Lloyd C. Wilson, medical director, state selective service board, spoke on medical preparedness. A symposium on tuberculosis was presented by Drs. Philip Batchelder, Joseph Smith, John I. Pinckney, John C. Ham, Providence, and Ubaldo E. Zambarano, Wallum Lake. Dr. Joseph V. Meigs, Boston, spoke, November 4, on "Female Endocrinology."

TENNESSEE

Chattanooga Clinical Congress.—The Chattanooga and Hamilton County Medical Society held its annual clinical congress October 31. The program of clinics was presented at the Newell Sanitarium in the morning and at the Erlanger Hospital in the afternoon. A banquet was held at the Hotel Patten in the evening with Drs. John Shelton Horsley, Richmond, Va., and Seale Harris, Birmingham, Ala., as the speakers on gastrointestinal surgery, including appendicitis, and "Insulin Jitters" respectively.

TEXAS

Appointments to Medical Faculty.—Dr. John J. Lawless, recently assistant professor of anatomy at the University of West Virginia School of Medicine, Morgantown, has been appointed assistant professor of anatomy at the University of Texas School of Medicine, Galveston. Dr. Lawless took a Ph.D. degree from the University of Minnesota in 1934 and an M.D. from Rush Medical College in 1939. He previously held a teaching fellowship at the University of Minnesota and an instructorship at Georgetown University, Washington, D. C. J. K. Kline, Ph.D., formerly research chemist with Merck and Company and the Bell Telephone Laboratories, has been appointed assistant professor in pharmacology, with special assignments in the department of preventive medicine and public health.

Annual Postgraduate Assembly.—The Postgraduate Medical Assembly of South Texas will hold its ninth annual clinical meeting, December 3-5, at the Rice Hotel, Houston. This meeting is a project of the eighth, ninth and tenth councilor districts of the State Medical Association of Texas. The speakers will be:

Dr. Horton R. Casparis, professor of pediatrics, Vanderbilt University School of Medicine, Nashville, Tenn.

Dr. Milton B. Cohen, director of the Asthma, Hay Fever and Allergy Foundation, Cleveland.

Dr. Claude C. Coleman, clinical professor of neurologic surgery, University of Virginia Department of Medicine, Charlottesville, and professor of neurologic surgery, Medical College of Virginia, Richmond.

Dr. James B. Costen, assistant professor of clinical otolaryngology, Washington University School of Medicine, St. Louis.

Dr. David M. Davis, professor of genito-urinary surgery, Jefferson Medical College, Philadelphia.

Dr. Charles C. Dennie, Kansas City, Mo., professor of clinical dermatology, University of Kansas School of Medicine, Kansas City.

Dr. John H. Dunnington, professor of ophthalmology, Columbia University College of Physicians and Surgeons, New York.

Dr. Sanford R. Gifford, professor of ophthalmology, Northwestern University Medical School, Chicago.

Dr. Byrl R. Kirklin, director, division of radiology, Mayo Foundation, Rochester, Minn.

Dr. Earl D. McBride, assistant professor of orthopedic surgery, University of Oklahoma School of Medicine, Oklahoma City.

Dr. Henry K. Mohler, dean and Sutherland M. Prevost professor of therapeutics, Jefferson Medical College, Philadelphia.

Dr. George Morris Piersol, professor of medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia.

Dr. Floyd T. Romberger, Lafayette Home Hospital, Lafayette, Ind.

Dr. Robert A. Ross, associate professor of obstetrics and gynecology, Duke University School of Medicine, Durham, N. C.

Dr. W. Likely Simpson, professor of otology, laryngology and rhinology, University of Tennessee College of Medicine, Memphis.

Dr. Harvey B. Stone, associate professor of surgery, Johns Hopkins University School of Medicine, Baltimore.

Dr. Howard C. Taylor Jr., William Goodell professor of gynecology, University of Pennsylvania School of Medicine, Philadelphia.

WEST VIRGINIA

Personal.—Dr. Maxwell F. Raine, Point Pleasant, district health officer for Mason, Jackson, Putnam and Roane counties, has been appointed health officer of Kanawha County to succeed Dr. Turner E. Cato, who recently went to Florida.

New Officers of Tuberculosis Association.—Dr. Leo H. Mynes, Charleston, was elected president of the West Virginia Tuberculosis and Health Association at the annual meeting in Clarksburg, September 19. Mr. E. P. Wells, field agent for the association, was appointed acting executive secretary to succeed the late George C. Rowell, Charleston, who died September 14.

HAWAII

Outbreak of Influenza.—Under date of October 4, Sr. Surg. Marion F. Haralson, Honolulu, reported to the U. S. Public Health Service an outbreak of influenza in the Territory of Hawaii, principally in Honolulu, with the occurrence of 1,800 cases and two deaths on the Island of Oahu since September 26. On October 13, Dr. Haralson reported a total of 4,298 cases with six deaths. He stated that the disease was of mild type, the cases averaging about three days of acute illness. For the two weeks ended October 19 and 26, respectively, there were 1,532 and 1,585 cases reported with no deaths. For the latter week, 725 cases were reported on the Island of Oahu. Influenza is not reportable in Hawaii except when officially declared to be epidemic, according to *Public Health Reports*.

GENERAL

Conferences on Therapy.—The therapeutic conferences developed at the Cornell University Medical College, New York, and first published as a series of special contributions in *THE JOURNAL* are to be continued during the present year in the *New York State Journal of Medicine*. The first of the new series will be concerned with the management of fever, the second with the treatment of nephritis. Since similar conferences are being developed in various medical schools, it has been suggested that this material now be published in state medical journals.

National Health Library Moves.—The National Health Library, administered by the National Health Council, announces its removal from the R. C. A. Building, Rockefeller Center, to 1790 Broadway, New York. This library now includes 6,000 volumes and 30,000 pamphlets and receives more than 500 medical and public health periodicals from all parts of the world. Although it is intended primarily for the use of the seventeen health organizations making up the council, individuals who are not members of the supporting organizations may have the privilege of using it for a small fee. A weekly index to the magazines is issued, also available to the public for a small annual subscription.

Jacobi Fellowship for Women Physicians.—The Women's Medical Association of New York offers a Mary Putnam Jacobi Fellowship for medical research of \$1,000, available Oct. 1, 1941, open to any woman doctor, either American or foreign, who is a graduate of a reputable medical school. Applications should be filed with the secretary of the committee by March 1, 1941, and must be accompanied by statements by persons other than the candidate as to (1) health, (2) educational qualifications and (3) previous work. The applicant herself should state the problem she proposes to investigate and send her photograph. The recipient will be expected to give full time to the study of her problem and to make a report for publication at the completion of her research. Application blanks may be obtained from the secretary of the committee, Dr. Phebe L. DuBois, 150 East Seventy-Third Street, New York.

Meeting of Radiologists.—The twenty-sixth annual meeting of the Radiological Society of North America will be held at the Hotel Statler, Cleveland, December 2-6. According to a preliminary program, the speakers will include:

- Dr. John R. Carty, New York, Soft Tissue Radiography.
- Drs. Ernst A. Pöhl and Lester W. Paul, Madison, Wis., Mediastinal and Pulmonary Changes in Erythema Nodosum.
- Dr. Max M. Peet, Ann Arbor, Mich., Ventrulography and Diagnosis of Brain Tumors.
- Dr. William S. Altman, Quincy, Mass., Cholangiography, Fractional Method.
- Drs. Walter C. Popp and Charles H. Watkins, Rochester, Minn., Effect of Roentgen Irradiation on Chronic Lymphatic Leukemia.
- Drs. Howard P. Doub, Jean P. Pratt and Horace C. Jones, Detroit, Combined Irradiation and Surgery in the Treatment of Carcinoma of the Pelvic Colon.
- Dr. Maurice D. Sachs, Portland, Ore., Carcinoma of the Male Breast: A Review of 200 Cases.
- Dr. Davis Spangler, Dallas, Texas, Effect of Roentgen Therapy on Closure of the Epiphyses.
- Dr. Ira I. Kaplan, New York, Irradiation Therapy of Brain Tumors.

Chinese Hospital Destroyed by Fire.—The Women's Hospital, connected with West China Union University, Chengtu on the Burma Road, was completely destroyed by fire following a Japanese air raid in August, according to a letter from Dr. Sven H. Liljestrand to the Board of Foreign Missions of the Methodist Episcopal Church. The fire destroyed all the cystoscopic and electrotherapeutic apparatus except one cystoscope that had been lent to another hospital unit, as well as all the medical periodicals. Dr. Liljestrand reported. If any physicians are interested in assisting him with second hand apparatus and used copies of journals, they are

asked to communicate with the Medical Department, Board of Foreign Missions, Methodist Church, 150 Fifth Avenue, New York. Dr. Liljestrand is a native of New York and graduated from Syracuse University College of Medicine in 1915.

Society News.—Dr. William M. Doughty, Cincinnati, was chosen president-elect of the American Roentgen Ray Society at its annual meeting, October 3, and Dr. Merrill C. Sosman, Boston, was installed as president. The next annual session will be held in Cincinnati, October 6-11. —At the recent meeting of the Association of Military Surgeons of the United States, Dr. James A. Mattison, Glendora, Calif., was inducted into the presidency. Col. James M. Phalen, U. S. Army, retired, Army Medical Museum, Washington, D. C., is the secretary. Louisville has been selected as the place for the next annual session. —The American Association of the History of Medicine held its first fall meeting in Cleveland, October 7. Among the speakers were Drs. David A. Tucker Jr., Cincinnati, "Daniel Drake, Pioneer Medical Educator of the Middle West"; Logan Clendening, Kansas City, Mo., "Memorials of Medicine in America" and Louis S. Deitchman, Youngstown, Ohio, "Early Medical Printing."

Census of Medical Manufactures.—According to preliminary returns from the census of manufactures for 1939, the value at the factory of surgical instruments and parts made last year was \$7,160,692. X-ray and therapeutic apparatus and electronic tubes had a factory value of \$17,886,322. Surgical supplies and equipment and orthopedic appliances aggregated \$71,679,980.

Statistics are not yet available on the 1939 output of drugs and medicines. In 1937, the value of drugs and medicines as reported by the manufacturers in that year's census was \$345,918,343.

Within the surgical supplies industry, a seemingly small item like surgical gut strings alone accounted for \$3,673,516 of production. Surgical gauze and dressings totaled \$12,510,508. Absorbent cotton production was valued at \$3,483,467. Non-medicated adhesive plasters had a value of \$5,946,645, while medicated plasters were produced to the extent of \$3,792,159. Bandages amounted to \$3,588,637. Sterilizers had a worth of \$1,153,680. The remainder of the industry's production is accounted for by items like artificial limbs, trusses, arch supports, surgical belts, and the like.

X-ray apparatus for general medical use had a value at the factory last year of \$8,260,750, plus \$2,112,942 for x-ray tubes. Ultraviolet health lamps were valued at \$1,150,221, while the infra-red totaled \$232,445. The value of high-frequency apparatus produced was \$1,324,978. Physical therapy equipment totaled \$1,378,232. Vibrators and other motor-driven devices were worth \$486,713. All other electromedical and electrotherapeutic apparatus, including electrocardiographs, amounted to \$1,212,339.

Production of surgical instruments and parts in 1939 was valued at \$7,160,692, as compared with \$5,830,430 in 1937. Clinical thermometers had a value of \$1,575,069. Of the \$3,831,225 total for laboratory instruments and apparatus, a substantial amount undoubtedly represents equipment for medical use.

There were fifty establishments primarily engaged last year in the manufacture of surgical and medical instruments, as compared with thirty-nine in 1937. They gave employment to 1,626 wage earners, who received a payroll of \$1,978,574. Salaried personnel numbered 319, with earnings of \$1,006,020. For materials, supplies, fuel, purchased electrical energy and contract work they spent \$2,319,720. In total value of products, they show a gain of 6.4 per cent over 1937.

In the classification of surgical supplies manufacturers, there were 360 plants last year against 323 in 1937. Their 8,468 wage earners received \$8,547,630, while salaried personnel numbering 1,967 had earnings of \$4,728,519. The industry paid out for materials, supplies and the like \$40,296,584. The value of its products rose 3 per cent over 1937.

The manufacture of x-ray and therapeutic apparatus in 1939 occupied eighty-four plants, compared with forty-six in 1937. They had 1,959 wage earners and 692 salaried employees, paying out \$2,744,251 in wages and \$1,815,337 in salaries. Cost of materials, supplies and the like was \$5,754,928. Value of their products increased 4.6 per cent over 1937.

CANADA

The Louis Gross Lecture.—Dr. Emanuel Libman, New York, delivered the third annual Louis Gross Memorial Lecture, November 20, at the Montreal Jewish General Hospital under the auspices of the Montreal Clinical Society. Dr. Libman's subject was "Endocarditis and 'Libman-Sachs' Disease'."

Foreign Letters

LONDON

(From a special correspondent)

Oct. 17, 1940.

An Air Raid in Harley Street

This is a quiet night after two unpleasant ones. I am writing to you in bed in my ground floor back room (which I prefer to the basement, where my family sleeps). I can hear the throbbing hum of an occasional German plane overhead and the quick thud-thud of our antiaircraft guns, but only at odd intervals. We in London have settled down to the queer sort of life we are living and have no intention of leaving it, quite why I don't know, for friends out of London are always urging us (and other people) to leave it, but mostly because one feels that if one leaves London the Germans have got us even that amount down, and we're not having that. The night before last was the first night I have actually got out of bed,

Street, and there are 152 houses in the street. We always feel that it might have been us or it might be us tonight, but one gets very fatalistic about it all and the casualties are really infinitesimal as compared with the damage done, and even that, though bad enough, is only a flea bite when you look at London as a whole. The population is as determined as ever not to flinch from the blows the Germans are giving us, and we know that we are now hitting them just as hard. I happened to turn the radio tonight by accident to the Bremer station, when the announcer we call "Lord Haw-Haw" (from his affected voice) was talking: his description of the last raid on London I knew from personal observation was perfect nonsense; why he had to exaggerate so ludicrously I can't understand for, of course, they have done some damage quite worth describing from his point of view; apparently he prefers absurd lies to the quite horrid enough truth, as a matter of policy.

I was in a tube (subway) yesterday for the first time for a long time and was much interested to see the quiet underground life that has sprung up among a large section of our population—a life with customs and laws of its own. I was there about 3:30 p. m. and already along the walls, in the subway stations, blankets, suitcases, folding chairs or pillows had been laid down in an orderly manner to reserve places. A few youngsters and old people were already in their places, prepared to stay there until the next morning, about 7 o'clock. Surface shelters have been provided pretty freely in all streets, but thousands of people prefer the comparative discomfort but warmth, light and freedom from noises of gun fire and bombs and the feeling of perfect safety deep down in the passages, stairways and station platforms of our underground railway. The government discouraged it and tried to make rules about it, but the population took matters into their own hands and made their own unwritten but strictly obeyed rules for this sort of thing.

Otherwise things go on as before. My telephone has been off (cables damaged by bombs) for a week, but water, gas and electricity are all right. No signs of shortage of food or any real essentials.

LONDON

(From Our Regular Correspondent)

Oct. 19, 1940.

Should There Be Nurse-Anesthetists?

The Association of Anesthetists has addressed to the chairman of the board of governors of Addenbrooke's Hospital, Cambridge, a letter of protest, signed by the members of the council, who are leading anesthetists, protesting against an advertisement for a nurse to be trained to act as an anesthetist in the hospital. The letter is the result of a meeting of the council specially convened to consider the matter. The council expressed grave misgiving at the advertisement and stated that it has been unable to trace any effort by the hospital to secure applications of qualified persons for the appointment. The institution of a nurse-anesthetist at a hospital of the standing of Addenbrooke's appears to the council to be a retrograde step which is injurious to the public welfare. It holds that the responsibility for a patient under an anesthetic cannot be safely entrusted to any one who is not medically qualified. As far as the anesthetic is concerned, the anesthetist has to bear the full responsibility, as has been frequently proved in the coroner's court. These duties cannot properly be assigned to an unqualified person. If they were and an accident befel the patient, public resentment would be aroused against the hospital concerned. The Royal Colleges of Physicians and Surgeons have recognized the specialty of anesthetics by granting a diploma. This advance has been due to the labors of medical men who devoted themselves to the study of anesthetics. Further progress can be achieved only by the encouragement of similar efforts. The



Harley Street in the battle of London. Three houses destroyed, the middle one that of Mr. Sampson Handley, the well known surgeon and authority on cancer. The snapshot shows how little the rest of Harley Street has been affected.

dressed fully, had my (already packed) suitcase handy and told the others downstairs to get their clothes on and prepare to leave the house at a minute's notice: we didn't actually have to, but from my window I could see a house only two away from us (round the corner) blazing away after an incendiary bomb, and another house about four or five the other side has had its back bombed and partly demolished. I thought the flames might reach us but they didn't, for our fire services are very efficient indeed and soon got it under control. I hope the censor allows the snapshot I have enclosed to pass: I took it a week or so ago from my front door and it shows what a bomb did that fell opposite: three houses in dust, like teeth pulled out, and several others badly damaged. You can see from the photograph that that is all the damage (so far) in Harley

council points out that in Canada, where the nurse-anesthetist was common, she has now been made illegal and that in the United States her existence is deplored by many of the best authorities. For England, which has in many ways been foremost in the advance of anesthetics, to take a backward step by encouraging unqualified anesthetists would be lamentable.

The staff of Addenbrooke's Hospital replied suggesting that "the grave misgiving" of the committee may be mitigated by the following facts: With the outbreak of war, five of the eight anesthetists of the hospital were mobilized, while the beds have been increased by more than 140 and another 150 are in contemplation. Some inexperienced anesthetists have had to be employed. At the present moment the training of students in administering anesthetics at the London hospitals cannot be ideal, and it is from these that resident anesthetists are drawn. The staff therefore considered the training of its own anesthetists. Some of them had considerable experience as sister-anesthetists in the United States and on the European continent, and a large hospital in England has employed them for years with entire success. To safeguard the interests of surgeon and patient it was decided that each sister-anesthetist should receive six months' training—double that required for a physician.

Butter Ration Reduced

At this season arrivals of butter from Australia and New Zealand are always at their lowest, rising from November with the advance of the summer months in the Southern Hemisphere. Normally this seasonal decline is made good by imports from Denmark and Holland, which are not now available. The minister of food has therefore decided as a precautionary measure to conserve stocks by reducing the butter ration from 4 to 2 ounces a week. But the present fat ration, which includes butter, margarine and cooking fats, will remain at 8 ounces. Thus the diminished butter ration can be compensated by increase of the other fats. As the margarine is vitaminized it is a complete substitute for butter. Another offset is that the meat ration (which is measured by expenditure) is increased from 44 to 50 cents a week. In a broadcast the minister of food has said "In this second year of the war you will have enough to eat, but I shall have to ask you to be prepared for changes for short periods."

ITALY

(From Our Regular Correspondent)

Sept. 15, 1940.

Hospitals in Albania

A project for the enlargement of hospitals functioning in Albania and for the construction of new hospitals with state funds was approved. New pavilions similar to those constructed in the Tyrana hospital will be built in the hospitals of Scutari, Koritza and Valona. In the Scutari hospital the enlargement of the hospital will begin immediately. X-ray equipment is already being established in the Scutari, Koritza and Valona hospitals. The Durazzo hospital will be enlarged to three times its capacity. Other plans for constructing a new hospital in Argirocastro and small hospitals in Kukes and Pesh Kopija and, later on, in Perat and Elbassan are being studied.

Prevention of Measles

Professor Petraghani, general director of public health, recently presented a report on the results of administering a phenolated placental extract which is used in the prevention of measles and known in Italy by the name of "Fenepla." In the Cosenza province the preparation was administered to sixty-seven children who had never had measles but who were exposed to the disease. It developed in six cases. Of seventy-four exposed children in the Reggio Emilia province who were vaccinated with the preparation against measles it developed in none. The author found the preparation valuable in preventing measles especially in schools, colleges and resorts for children.

Congress of Dermatology and Syphilology

At the recent meeting of the thirty-second National Congress of the Società Italiana di Dermatologia e Sifilografia in Bologna Prof. Leonardo Martinotti presided. The first official topic was "Subacute Inguinal Lymphogranuloma." Professor Cerutti reviewed the literature on experimental transmission of the infection. Granular corpuscles exist in the tissues in all cases; whether they represent the true virus of the infection has not been proved. Professor De Giorgio discussed the preparation of antigens for Frei's intradermal reaction. Professor Midana discussed extraglandular forms of the infection.

The second official topic was "Cutaneous Tuberculosis." Professors Bergamasco and Cibiriani reviewed the statistics for Italy, by which they showed that the disease had diminished during the last ten years. Professor Pinetti reviewed the literature on the various forms of tuberculous ultravirus, which, according to him, is not the pathogenic factor of cutaneous tuberculosis: Professor Scolari spoke on the evolution of tuberculin allergy and the desensitizing factors. Professor Lisi discussed experimental cutaneous tuberculosis. Professor Klarer discussed the relations between allergy and immunity in the production of organic reactions of defense and the type of reactions connected with cutaneous tuberculosis. Professor Bertoncini spoke on lupus vulgaris. Professor Versari spoke on the treatment of cutaneous tuberculosis with special reference to climate, heliotherapy, proper diet, local chemical therapy, and local and plastic surgery. The election of president for the society resulted in the reelection of Prof. L. Martinotti.

Deaths

Senator Giuseppe Tusini, professor emeritus of the surgical clinic at Genoa University, is dead. He published books and articles, some of which were "Echinococcosis of the Liver," "Varieties of Endothelia," "Actinomycosis of the Foot," "Chronic Polyadenopathy in Relation to Glanders in Pathogenesis," "Lymphatic Varicocele from Filariasis" and "Cysts and in Tumors of the Pancreas." He was the originator and founder of the Castrensian University during the war of 1914-1918. It was established near the front for students of medicine and surgery who were at the front and who attended the university during rest periods in winter.

Marriages

CHARLES BRUCE KERN, Lafayette, Ind., to Mrs. J. Cooper Props of Muncie, at Harrodsburg, Ky., October 4.

JOSEPH GORDON, Ray Brook, N. Y., to Miss Beatrice Brecker of Brooklyn at Plattsburg, N. Y., October 26.

RUSSELL K. HORSMAN, Kokomo, Ind., to Miss Lotte Nevella Benedick at Manhattan, Kan., September 28.

WILBUR GEORGE DOWNS, Saranac Lake, N. Y., to Miss Helen Hartley Geer of New York, September 14.

WILLARD A. PRICE, Nappanee, Ind., to Miss Nellie R. Coppes of Denver, at Crete, Neb., in September.

LAWSON J. CLARK, Indianapolis, to Miss Mildred Harting of North Manchester, Ind., October 11.

CLARENCE C. BOSSELMANN to Miss Clementine Foster, both of Fort Wayne, Ind., October 5.

LYMAN D. EATON to Miss Alberta Marie Speicher, both of Indianapolis, October 12.

MILTON A. SPITZ, St. Louis, to Miss Lucille Lesch of Madison, Wis., October 6.

IVAN CARLYLE, Sedalia, Ind., to Mrs. May Kingery of Middlefork, October 9.

FAY F. BOYS to Miss Jean Sopko, both of East Chicago, Ind., September 28.

JOHN D. COLLINS to Miss Mary Johnston, both of Seattle, in August.

Deaths

William Lawrence Estes ☉ Bethlehem, Pa.; University of Virginia Department of Medicine, Charlottesville, 1877; University of the City of New York Medical Department, 1878; member of the House of Delegates of the American Medical Association in 1909; member of the American Surgical Association; lectured on physiology and hygiene at Lehigh University from 1883 to 1923; fellow of the American College of Surgeons; served in various capacities on the staff of St. Luke's Hospital; in 1934 received the honorary degree of doctor of science from Lehigh University; aged 84; died, October 20, of coronary sclerosis with occlusion.

Nathaniel Hawley Brush ☉ Santa Barbara, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1914; member of the American Psychiatric Association and the Association for Research in Nervous and Mental Disease; past president of the Santa Barbara County Medical Society; served during the World War; instructor of psychiatry at his alma mater from 1916 to 1918; on the staff of the Santa Barbara Cottage Hospital and the Santa Barbara General Hospital; aged 53; died, October 21, of carcinoma of the pancreas and biliary obstruction.

Henry Wellington Yates ☉ Detroit; Detroit College of Medicine, 1894; emeritus professor of gynecology and obstetrics at his alma mater, now known as the Wayne University College of Medicine; fellow of the American College of Surgeons; past president of the Wayne County Medical Society and for many years chairman of the cancer committee; gynecologist, Providence and William Booth Memorial hospitals; consultant in gynecology, Woman's Hospital; formerly member of the city plan commission; aged 73; died, October 13, in the Harper Hospital of bronchiectasis and arteriosclerosis.

Joseph A. Estopinal, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1899; member of the Louisiana State Medical Society; at one time secretary of the state board of health; served during the World War; formerly medical inspector of public schools in St. Bernard Parish; at one time professor of laryngology and rhinology, New Orleans Post-Graduate School of Medicine; on the staff of the Illinois Central Hospital; formerly on the staff of the Eye, Ear, Nose and Throat Hospital and the Charity Hospital; aged 64; died, October 9.

Henry Carlton Courten ☉ Richmond Hill, N. Y.; University and Bellevue Hospital Medical College, New York, 1909; fellow of the American College of Surgeons; attending orthopedist to the Jamaica, Queensboro, Lutheran and Mary Immaculate hospitals, Jamaica; visiting orthopedist to the Queen's General Hospital, Jamaica; consulting orthopedic surgeon, Rockaway Beach (N. Y.) Hospital, Evangelical Deaconess Hospital, Brooklyn, and the Flushing (N. Y.) Hospital; past president of the Medical Society of the County of Queens; aged 61; died, October 15.

John P. Munroe, Charlotte, N. C.; University of Virginia Department of Medicine, Charlottesville, 1885; member of the Medical Society of the State of North Carolina; member of the House of Delegates of the American Medical Association in 1915; fellow of the American College of Physicians; past president of the Mecklenburg County Medical Society; formerly professor of neurology and practice of medicine, North Carolina Medical College; president and member of the staff of the New Charlotte Sanatorium; aged 83; died, October 14, of pneumonia.

Torr Wagner Harmer ☉ Boston; Harvard Medical School, Boston, 1907; member of the American Association for the Surgery of Trauma and the New England Surgical Society; fellow of the American College of Surgeons; instructor in anatomy and assistant in surgery at his alma mater; consulting surgeon at the Massachusetts Eye and Ear Infirmary and at the Somerville, Winchester, Symmes Arlington and Waltham hospitals; aged 59; died, October 2, of carcinoma.

Roy Jones Holmes ☉ Miami, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1917; past president of the Dade County Medical Society; member of the American Urological Association; fellow of the American College of Surgeons; chief surgeon, urologic division, James M. Jackson Memorial Hospital; visiting urologist, Victoria and Dade County hospitals; aged 46; died, October 9, of acute coronary thrombosis.

Francisco Jose Hernandez ☉ San Juan, P. R.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; professor of clinical pathology at the School of Tropical Medicine of the University of Puerto Rico, under the auspices of Columbia University; on the staff of the Sanatorio de la Sociedad Española de Auxilio Mutuo y Beneficencia, Rio Piedras; aged 58; died, October 4, of heart disease.

Ovid Clemmons Foote ☉ Surgeon Lieutenant Commander, United States Navy, retired, Washington, D. C.; Johns Hopkins University School of Medicine, Baltimore, 1912; member of the American Urological Association; entered the navy in 1914; served during the World War; retired in 1924 for incapacity resulting from an incident of service; aged 53; died in October of injuries received in an automobile accident.

Guy Hunt Cochran ☉ Los Angeles; Columbia University College of Physicians and Surgeons, New York, 1900; member of the Pacific Coast Surgical Association; fellow of the American College of Surgeons; aged 67; chief of staff of Children's Hospital from 1915 to 1937; for many years on the attending staff of the Hospital of the Good Samaritan, where he died, October 7, of carcinoma of the bronchus.

Walter William Propst ☉ Scranton, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1916; past president of the Lackawanna County Medical Society; served during the World War; at various times on the staff of the West Side, Scranton State and Mercy hospitals, Scranton, and the Mid-Valley Hospital, Peckville; aged 55; died, October 11, of pneumonia.

Nicholas Francis Brecker, Philadelphia; Medico-Chirurgical College of Philadelphia, 1907; member of the Medical Society of the State of Pennsylvania; on the staffs of the Presbyterian and the Philadelphia General Hospital; aged 58; died, October 11, of acute coronary occlusion.

Lewis Gordon Allbritton, Birmingham, Ala.; Indiana University School of Medicine, Indianapolis, 1928; member of the Medical Association of the State of Alabama; aged 40; died, October 4, in the Johns Hopkins Hospital, Baltimore, of glioma and spongioblastoma multiforme.

Alexander Donald Ferguson, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; served during the World War; aged 54; died, October 14, of injuries received when he was struck by an automobile.

Jesse Ira Whittenberg, Louisville, Ky.; Kentucky School of Medicine, Louisville, 1894; formerly county coroner and health officer; served with the United States Public Health Service during the World War; aged 68; died, September 24, of carcinoma of the throat.

Adelbert Boyd Miller ☉ Erie, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1905; past president of the Erie County Medical Society; served during the World War; aged 59; president of the staff of the Hamot Hospital, where he died, September 11.

Rudolph Clarence Pfeil ☉ Milwaukee; Milwaukee Medical College, 1908; served during the World War; on the staffs of the Johnston Emergency Hospital and St. Luke's Hospital; aged 57; died, October 3, of carcinoma of the pancreas.

George Washington Anglin, Warsaw, Ind.; Northwestern University Medical School, Chicago, 1905; member of the Indiana State Medical Association; served during the World War; aged 66; was drowned, September 15.

Morris Bander, New York; University and Bellevue Hospital Medical College, New York, 1925; physician in the men's hygiene department, Brooklyn College; aged 39; died, October 22, of coronary thrombosis.

Frederick Da Costa Austin, Charlotte, N. C.; North Carolina Medical College, Charlotte, 1907; county coroner; aged 54; died, October 14, in the Mercy Hospital of cerebral hemorrhage and chronic nephritis.

Walter R. Coryell, St. Louis; American Medical College, St. Louis, 1878; aged 86; died, October 10, in the Alexian Brothers Hospital of injuries received in a fall.

Rene Plamondon, Quebec, Que., Canada; Laval University Faculty of Medicine, Quebec, 1906; aged 56; died, August 21.

Correction.—Since publication of a statement concerning the relationship of Dr. John T. Hodgen, former President of the American Medical Association, and the late Dr. William Allen Pusey, in THE JOURNAL, October 12, further correspondence from relatives and friends shows that Dr. Hodgen was a second cousin to Dr. Pusey.

Correspondence

MEDICAL CONTROL OF MOBILIZATION

To the Editor:—In an editorial entitled "The Medical Control of Mobilization" in *THE JOURNAL*, October 12, it is stated that "Much control over the epidemic intestinal diseases such as typhoid and dysentery can be exerted by suitable preventive measures, but the situation with regard to respiratory diseases is more difficult. In such conditions as measles and mumps neither prevention nor treatment can be much better controlled than formerly."

I am under the impression that the use of immune globulin and convalescent serum in measles and of convalescent serum in mumps has become firmly established as of great value in the prophylaxis of these diseases. Certainly in hospital practice we no longer have the terror of measles running through our wards at will as it used to do, and it would seem to me that by establishing depots of suitable convalescent serum the same situation would hold in army camps.

By inoculating all the susceptible in the same building one surely should cut down the spread of these diseases to a minimum.

Of course large amounts of convalescent or immune serum would be necessary, but we all know of centers in New York and elsewhere where such is already the case. It would seem that establishing such facilities should be one of the important adjuncts of mobilization.

CHARLES F. WALCOTT, M.D., Cambridge, Mass.

CLOSED METHOD OF TREATING COMPOUND FRACTURES

To the Editor:—The editorial (*THE JOURNAL*, September 21) devoted to the "Closed Method of Treating Compound Fractures and Infected Wounds" stirs me to add a few words to the discussion. These words have been repeated many times during the past fifteen years, becoming somewhat of a habit, harmless but perhaps boring. They run as follows:

The elements of this method were erected into a doctrine sometime before 1885 by Leopold Ollier of Lyons. He called it simply "delayed dressings" and then elaborated on the technic in much the same terms that are employed today, plaster, odor and all. Some of the credit for his ideas he assigned to Langenbeck and to Poncet. Since then his doctrine has been quite faithfully followed by the Lyoneses, in theory and in practice. Mention in the literature is rare because the ideas involved are taken for granted by the heritors of the Ollier tradition. Besides, the aloof, dour old town, birthplace of Emperor Claude, a "free city" for ages, home of Rabelais and Dolet, haven of Calvin and Servetus, disdains advertising anyhow. But a special application of the method to the treatment of compound fractures with delayed union was advanced by Louis Tixier in 1917, both in the literature and before groups of American surgeons, and it was also discussed by Jean Haour in a thesis about 1925.

As a consequence of the foregoing, I once again urge that the method be associated with the name of Ollier. Any one familiar with the monumental "Traité des resections" or with the surgical practices of the Lyons school will agree that in this way the memory of the "distinguished surgeon of Lyons" (Senn) will be justly honored. Moreover, the method will receive a convenient appellation. Ollier's own term is inadequate and the one used by *THE JOURNAL* is cumbersome. Therefore let it be "Ollier's Method."

ALBERT DE GROAT, M.D., Detroit.

CHRONIC NEPHRITIS AND LEAD POISONING

To the Editor:—I have read with interest your leading article in *THE JOURNAL* of May 4 on my book on "Chronic Nephritis and Lead Poisoning." This book was published seven years ago, and since that date the Queensland government has brought in stringent legislation against the use of lead paint in places accessible to children. This action was taken after my observations had been fully investigated. Much more confirmatory work has been carried out by Dr. Gilbert Murray and his co-workers of the Commonwealth Health Department and by Dr. E. H. Derrick of the Queensland Health Department.

Owing to the new legislation these cases will soon become a rarity, and it is tragic that such splendid research material is being entirely neglected because, owing to war activities here, no one is able to devote time to the further investigation of this very important question, which will almost certainly throw new light on the etiology of many cases of arteriosclerosis.

If an American research organization could send out a skilled researcher I feel sure that in two years he would be able to collect sufficient evidence to write a new chapter on vascular sclerosis. Those of us who have studied this question in Queensland can state dogmatically that in this climate chronic lead poisoning in childhood, when sufficiently severe to cause paralysis, is almost invariably followed by arteriosclerosis and chronic nephritis in early adult life. Most of Queensland is situated within the tropics, and it is my belief that the heat factor plays some part in this morbid process.

You can be assured that herein is a remarkable opportunity for research for which very little funds would be needed.

As the cases are fast disappearing I feel that it would be most unfortunate if this exceptional opportunity were neglected. Can you help?

L. J. JARVIS NYE, M.B., CH.M., F.R.C.P.,
Queensland, Australia.

"ELECTRICAL CONVULSION TREATMENT OF MENTAL DISORDERS"

To the Editor:—In the editorial in *THE JOURNAL*, August 10, on "Electrical Convulsion Treatment of Mental Disorders," credit was accorded to Cerletti for first utilizing the electric current in 1937 to induce epileptic seizures in animals. I should like to call attention to a paper by Clark and Wall (Unconsciousness Produced by Electric Currents, *Quart. J. Exper. Physiol.* 24:85 [Feb.] 1934) which states that in 1900 Leduc, by applying certain types of current to an animal's head, produced a fit with loss of consciousness varying in degree from a condition resembling sleep to one of deep coma and loss of reflexes but without causing any permanent damage to the animal.

Robinovitch (Sommeil électrique, Nantes, 1906) also described a condition in animals which she called "épilepsie électrique" and in which loss of consciousness was associated with many features characteristic of the epileptic fit. Weiss (*Bull. Soc. Internat. des Elect.*, Paris 1:417:1911) and Hess (*Compt. rend. Soc. de biol.* 107:1333 [Aug. 5] 1931) confirmed these results.

Clark and Wall showed that (1) animals displayed no fear of repeated shocks and seemed quieter and more docile for a considerable time after treatment; (2) an initial fall in blood pressure occurred which was abolished by section of the vagi; (3) by direct observation through a window in the skull the cerebral vessels were constricted, followed by dilatation after the current was switched off, and (4) direct cerebral stimulation and not vasoconstriction of the cerebral vessels was responsible for the convulsions, since stimulation of the proximal

end of the cervical sympathetics, while producing vasoconstriction, did not elicit an epileptiform seizure.

I trust that these references will add to the experimental background of the electroconvulsive therapy.

WILLIAM FURST, M.D., Philadelphia.
Philadelphia General Hospital.

USE AND ABUSE OF ADVERTISING BROCHURES

To the Editor:—Your editorial in *THE JOURNAL*, October 5, entitled "Use and Abuse of Advertising Brochures" calls attention to a condition which results in serious economic waste, waste of the recipient's time in inspecting and disposing of unwanted brochures, waste in material and postage on the part of the sender, and waste in the way of an unnecessary tax on the postal facilities of the government.

Besides the example noted in your editorial of the doctor who had received over 300 pounds of such matter in about a year's time, I recall an example in which during an absence of two months there came to a doctor's office 16½ pounds, or 222 pieces, of such material, of which not more than 5 per cent was of any possible interest to him.

This wasteful condition will be remedied if recipients will (1) Write "Refused" or "Not accepted" above address, (2) draw a line through but leave legible the name and address and (3) remail.

The brochure will then be returned to the sender, who will pay the return postage and will or should revise his mailing list.

W. E. CARSON, M.D., Pittsburgh.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

NEPHROSIS OR NEPHRITIS

To the Editor:—What diet and medication can be suggested for an 18 year old youth with considerable swelling of the face, rales throughout the lung fields, swelling of the ankles and possibly slight fluid accumulation in the abdomen? The heart sounds are of normal quality, rate and rhythm; there is normal temperature; the blood pressure is 160 systolic, 110 diastolic; the specific gravity of the urine is 1.010 and the urine is almost solid with albumin. There are no casts, blood or pus. The urea nitrogen is 20.2 mg., urea clearance 63 per cent, hemoglobin 52 per cent, red cells number 2,980,000, white cells 6,800. There is a normal differential count. The tonsils were removed years ago and there appears to be no other source of infection. Is this more of a nephrosis than nephritis? Would it be advisable to give salyrgan? M.D., New Jersey.

ANSWER.—Whether or not a condition of pure nephrosis or a nephrotic syndrome of Bright's disease or both exists is at present the subject of much discussion. Nevertheless the nephrotic picture in its purer forms is definitely an entity, and its diagnosis and treatment differ from that of nephritis. In addition to the features mentioned in the query there are constantly present in nephrosis elevation of blood cholesterol to levels frequently above 300 mg. (this being the only increase in blood chemistry) and a definite lowering of plasma protein, the albumin fraction to a greater degree than globulin, resulting in a reversal of the albumin:globulin ratio. Blood pressure is usually within normal limits and elevation of the degree noted indicates vasoconstriction, which may result in renal ischemia with ultimate insufficiency and a clinical picture more of the uremic type.

However, the process rarely reaches this stage, since recovery takes place or death occurs from intercurrent infection. A great point of difference between nephritis and so-called pure nephrosis is that patients with the latter succumb to a pure nephrosic infection, commonly pneumococcal peritonitis; in fact, some writers state that they have observed only this cause

of death in such cases. Among the commonest causes of onset or recurrence is chilling. The diagnosis in this case would probably be nephrosis. When tubular damage exists, the use of mercurial diuretics such as salyrgan is not advised. The xanthine derivatives, especially theophylline and theobromine and their derivatives may be used (Marvin, H. M.: *Therapy of Dropsy*, *THE JOURNAL*, March 2, 1940, p. 757). More important is the fact that the edema is due to decrease of osmotic pressure of the blood resulting from loss of plasma protein. A common fault in treatment is inadequate protein in the diet. This may be administered in any form, but meat should furnish a large portion of the protein. Quantitatively, three needs must be fulfilled: (1) the daily requirement which by liberal calculation may be 1 Gm. per kilogram of dry weight, (2) renal loss, often from 20 to 30 Gm. daily, and (3) reserve for building up the depleted plasma proteins. This amount is arbitrary and may be increased until the total approximates the patient's tolerance. It should be borne in mind that a gram of meat, for example, does not represent a gram of protein.

Absolute restriction of sodium is necessary in nephrosis. This means no salt, sodium bicarbonate or alkaline preparations. The dietary management is most difficult since a daily diet containing 3 Gm. or less of salt is almost a problem for quantitative diet experts. Butter must be unsalted, no milk is permitted and bread must be specially prepared without salt, in addition to avoiding all salting of other food and avoiding salt-containing food, potato chips and the like. Potassium chloride 3 Gm. given daily to be used as salt on food or in 0.5 Gm. coated tablets may be used. There is no need for undue fluid restriction, as edema is influenced by factors other than water intake. Other than this, rest, warmth and other general measures may be indicated.

ONE HOUR-TWO DOSE DEXTROSE TOLERANCE TEST

To the Editor:—What is the significance of the sugar tolerance test which is completed in one hour by the following method: 1. Collect specimen of urine and blood and administer 50 Gm. of dextrose. 2. In one half hour repeat. 3. In another half hour collect a third specimen of blood and urine. How can this test prove or disprove a diabetic blood sugar curve, when the essential diagnostic point is the return of the blood sugar to normal in two to three hours in the nondiabetic and the lack of return in the diabetic? Kindly discuss, especially in its application to the diagnosis of renal glycosuria. M.D., Ohio.

ANSWER.—The test described is the one hour-two dose procedure devised by Exton and Rose. It is based on the well known Hamman-Hirschman (Staub-Traugott) effect: the administration of dextrose to a normal individual sets in motion certain processes (probably in the liver and pancreas) which make it easier for the body to utilize a second amount of dextrose given a short time later so that the peak of a second blood sugar curve is lower than that of the first; in a diabetic individual, however, the second dose gives rise to still more pronounced hyperglycemia.

Exton and Rose outlined criteria of diagnosis which depend chiefly on the height and extent of the blood sugar curve during the second half hour as opposed to that during the first. These criteria have been analyzed by Matthews, Magath and Berkson, who reported recently on results with the Exton-Rose test in a series of 117 normal persons and 304 individuals diagnosed clinically as diabetic. They conclude that the most reliable figure obtained is the hour value for the blood sugar and suggest that the half-hour value be dispensed with. They regard 158 mg. per hundred cubic centimeters for the hour value as a critical level; individuals with a reading below this point are regarded as nondiabetic and those with values at or above this value are designated as presumptively diabetic. The diagnosis of diabetes is thought definite if the hour value is 180 mg. or above.

These conclusions make one wonder whether it is profitable to divide the 100 Gm. of dextrose into two doses as advised by Exton and Rose, since the revised procedure suggested by Matthews and his co-workers returns closely to that of the standard dextrose tolerance test. These workers suggest two possible advantages of the divided dose even though only the fasting and the hour values are obtained: dividing the dose avoids the necessity of taking an unpleasantly large amount of sugar at one time and possibly brings out more clearly the divergence of the diabetic from the normal response.

The only significant difference between the response of the individual with renal glycosuria and that of the normal person is that the former will exhibit glycosuria throughout the test or at least after the administration of dextrose.

It must be borne in mind that, in the Exton-Rose test as well as in the standard sugar tolerance test, interpretation of the results will vary depending on whether venous or capillary blood samples are taken; capillary values will, in the normal person, be from 10 to 50 mg. higher after dextrose than the corresponding venous figures. Furthermore any of the conditions, such as previous restriction of carbohydrate, previous administration of insulin or infections, will influence the Exton-Rose just as they will the standard sugar tolerance test.

References:

- Exton, W. G., and Rose, A. R.: *Proc. A. Life Insur. M. Dir. America* 18: 252, 1931; *Am. J. Clin. Path.* 4: 381 (Sept.) 1934.
Hamman, Louis, and Hirschman, I. I.: *Bull. Johns Hopkins Hosp.* 30: 306 (Oct.) 1919.
Staub, H. A.: *Biochem. Ztschr.* 118: 93, 1921.
Traugott, K.: *Klin. Wchschr.* 1: 892 (April 29) 1922.
Soskin, Samuel; Allweiss, M. D., and Cohn, D. J.: *Am. J. Physiol.* 109: 155 (July) 1934.
Ricketts, H. T.: *J. Clin. Investigation* 17: 795 (Nov.) 1938.

EXTRAGENITAL SERONEGATIVE PRIMARY SYPHILIS

To the Editor:—A chancre of the finger, diagnosed by finding spirochetes seventeen days after the lesion first appeared, healed rapidly after treatment started. Blood tests were negative. 1. If the patient remains seronegative and without further symptoms or signs and continues treatment, what is the likelihood of transmitting the disease and by what manner and for how long a period after the initial lesion has healed? 2. What would you consider adequate treatment? 3. What do surgeons usually do about continuing work? M.D., Republic of Panama.

ANSWER.—1. If this patient with extragenital seronegative primary syphilis remains seronegative as to blood spinal fluid during one year of continuous antisyphilitic treatment, the risk of transmitting the infection to others from any ordinary daily contact is practically nil. For the complete protection of others, sexual intercourse should be completely avoided for the first six months of treatment; during the second six months it may be resumed with condom protection during the arsenical phases of therapy only; during the ensuing year of probation, it may be permitted with condom protection. Unrestricted sexual intercourse should not be permitted until completion of one year of post-treatment probation. Moist kissing should also be avoided for the year of treatment and the year of probation.

2. Adequate treatment consists of courses of an arsphenamine alternating with courses of a bismuth compound by the continuous system, no rest period being permitted, carried out during a full year of seronegativity of the blood. The system, drugs and dosage should be those suggested by the Cooperative Clinical Group.

3. There is no objection to a surgeon continuing work, though of course he should always wear rubber gloves during any surgical procedure, no matter how minor.

MORPHINE AND PROSTIGMINE IN PERITONITIS

To the Editor:—Would you explain the effects of prostigmine and morphine in peritonitis. M.D., New Jersey.

ANSWER.—Morphine and prostigmine are of value in ileus in that they both increase the intestinal tone. In peritonitis, prostigmine preferably should not be used, because it not only increases the intestinal tone but also increases peristalsis, which is undesirable in peritonitis in that the protective adhesions are likely to be broken down. Whereas prostigmine is of value in adynamic ileus not associated with peritonitis, it should not be used in adynamic ileus associated with peritonitis because of the reasons given. On the other hand, morphine is the ideal drug for use in peritonitis. It increases the intestinal tone without increasing peristalsis. In this way it overcomes the deleterious effect of intestinal dilatation incident to the adynamic ileus associated with peritonitis and at the same time does not favor the spread of peritonitis by breaking down the protective adhesions. Opium and its derivatives have been used for decades in the treatment of peritonitis. Standard treatment of typhilitis has long consisted of massive opianization. It has been previously thought that opium splinted the bowel and relaxed it, whereas in reality opium and its derivatives actually increase the tone of the bowel, and it is because of this action that morphine is beneficial in peritonitis. The dose of morphine depends on the age of the patient. For an adult from 0.016 to 0.02 Gm. (one-fourth to one-third grain) may be given every three to four hours. The patient should be kept narcotized with the drug. Because of its depressing effect on the respiratory center, it is desirable to give oxygen. Oxygen also has a definite decompressive effect on the intestine in that the inhalation of high concentration of oxygen favors the absorption of nitrogen from the intestine.

FRACTURE OF TUBEROSITY OF TIBIA AND ARTHRITIS

To the Editor:—A woman aged 54 suffered a twisting injury of her right knee. X-ray examination shows a compression fracture of the lateral tuberosity of the tibia. Treatment as advised by a specialist consists of an open operation elevating the compressed cartilaginous surface of the tuberosity and supporting it in its elevated position by means of bone blocks taken from the ilium or lower down in the tibia. The patient has had a preexisting degenerative arthritis involving among other joints the injured knee. I would appreciate a discussion of the possibility of the arthritis predisposing to the fracture and references in regard to the prognosis following surgery and as to the prognosis as regards the disability if surgery is refused. M.D., Washington.

ANSWER.—There is little evidence to be found in medical literature which would suggest that chronic arthritis is a predisposing factor in the production of fractures. Occasionally osteoporosis associated with arthritis may be a predisposing factor in the production of joint surface infarctions. This has occurred in osteomalacia or hyperparathyroidism in a number of reported cases. The recommendation to elevate the depressed cartilaginous surface of the tuberosity of the tibia is definitely in accord with the best surgical practice.

If the underlying bone is badly crushed or atrophic, introduction of a bone block would be indicated. Not uncommonly it is also advisable to remove the semilunar cartilage which may be torn or displaced as an additional complication in injuries of the type described.

As is well known, trauma to a joint with or without fracture is likely to produce some permanent loss of function. Because of the history of a preexisting degenerative arthritis the prognosis in this case, regardless of treatment, should be reserved.

SUGAR IN MEDICINES USED BY DIABETIC PATIENTS

To the Editor:—A problem that is arising with increasing frequency is the question of sugar content in various products used by patients with diabetes mellitus. For instance, the covering of one well known brand of ferrous sulfate is quoted by the manufacturers themselves as containing 6½ grains of sugar. Patients frequently ask about the sugar content of tooth powders and pastes, the powder used in causing adherence of dental plates and the like. Is it advisable to be particularly strict in the use of such preparations and is there a likelihood of disturbed control? M.D., Illinois.

ANSWER.—The quantity of sugar or other forms of carbohydrate on or in pills and medical powders is so insignificant as compared with the total carbohydrate in the diet as to be negligible. This does not hold for various liquid medicines in which sugar is sometimes present in large amounts.

If one of the pills mentioned does contain 6½ grains (0.4 Gm.) of sugar, two would contain even less than a gram, and six a day 3 Gm., which would be only one fiftieth of the usual amount of carbohydrate in the diabetic diet.

DANGERS FROM ENAMELWARE

To the Editor:—In *Queries and Minor Notes* in the August 31, issue of *The Journal* a question was asked on ill effects reported from chipped particles of enamel. Although the question seems to indicate an interest in possible physical damage, the answer includes possible chemical injury. The answer does not include a discussion of the possibility of antimony poisoning. It is rather common knowledge that antimony is used by many kitchenware manufacturers, sometimes in rather high concentrations in the production of kitchenware. The antimony gives a more opaque enamel and permits thinner application over the metal, which makes it desirable from the enamelers' standpoint. In cheap enamelware, however, acid foods extract this antimony and there is a definite danger of poisoning to any one eating such food. There are recorded outbreaks of this kind. Under these circumstances enamelware cannot be given an unqualified "clean bill of health."

G. I. Wallace, Ph.D.,
Department of Bacteriology, University of Illinois,
Urbana, Ill.

AGGLUTINATION WITH DYSENTERY BACILLUS

To the Editor:—In *The Journal* for October 19, there appears an inquiry concerning "Agglutination with Dysentery Bacillus." In the answer it is stated that the patient who has an agglutination which was typical for 1:160 with dysentery bacilli of the Flexner type has had a previous bacillary dysentery infection. Although this interpretation of the dysentery agglutination test holds true in many cases, it should be emphasized that a positive Flexner agglutination may be obtained in patients who present neither history nor evidence of Flexner dysentery. Certain individuals may have a relatively high titer of normal agglutinins for Flexner dysentery bacilli. Also the particular technic employed in setting up the test (time and temperature of incubation, and so on) may materially influence the result. Furthermore, because of antigenic relationship of the Flexner group of dysentery bacilli to other micro-organisms, for instance *B. alkalescens*, patients infected with the latter organism may have agglutinins in their serum giving a positive agglutination with Flexner dysentery bacilli. Erwin Neter, M.D., Buffalo.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, November 16, page 1744.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 17-19. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, Dec. 11. Sec., Dr. Charles B. Pinkham, 1020 N. St., Sacramento.

COLORADO: * Denver, Jan. 7-10. Applications must be on file not later than Dec. 23. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: * *Endorsement*, Hartford, Nov. 26. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden.

DELAWARE: July 8-10. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

GEORGIA: Atlanta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 8-11. Sec., Dr. James A. Morgan, 48 Young Building, Honolulu.

IDaho: Boise, April 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 335 State Capitol Bldg., Boise.

ILLINOIS: *Written*, Chicago, Jan. 21-22. *Reciprocity*, Chicago, Jan. 23. Supt. of Registration, Dept. of Registration and Education, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 17-19. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, Citizens Trust Bldg., Fort Wayne.

IOWA: Des Moines, Dec. 9-11. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, Dec. 3-5. Sec., State Board of Health, Dr. A. T. McCormack, 620 Third St., Louisville.

MARYLAND: *Regular*, Baltimore, Dec. 10-13. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homopathic*, Baltimore, Dec. 10-11. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: * Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: * Minneapolis, Jan. 21-23. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity*, Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: *Reciprocity*, Helena, March 31. *Written*, Helena, April 1. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: *Reciprocity with oral examination*, Feb. 3. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: Concord, March 13-14. Sec., Board of Registration in Medicine, Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, June 17-18. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 14-15. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 27-30. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, State Education Department, 315 Education Bldg., Albany.

NORTH CAROLINA: *Reciprocity*, Durham, Dec. 10. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: Columbus, Dec. 9-12. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, Dec. 11. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: * Portland, Jan. 14-16. Exec. Sec., Miss Lorraine M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia, January. Acting Sec., Bureau of Professional Licensing, Miss Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, Jan. 2-3. Sec., Division of Examiners, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH DAKOTA: * Pierre, Jan. 21-22. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

TEXAS: Austin, Nov. 25-27. Sec., Dr. T. J. Crowe, 918-920 Mercantile Bldg., Dallas.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 4-6. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WASHINGTON: * Seattle, Jan. 13-15. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WISCONSIN: * Madison, Jan. 14-17. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, Feb. 3-4. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, Dec. 17. Sec., Dr. Robert L. Nugent, University of Arizona, Science Hall, Tucson.

CONNECTICUT: Feb. 8. Address State Board of Healing Arts, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, April 21-22. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

IOWA: Des Moines, Jan. 14. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor, Detroit and East Lansing, Feb. 14-15. Sec., Miss Flora E. Dube, East Lansing.

MINNESOTA: Minneapolis, Jan. 7-8. Sec., Dr. J. Charnley McKinley, University of Minnesota, 126 Millard Hall, Minneapolis.

NEBRASKA: Omaha, Jan. 14-15. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, Feb. 15. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

SOUTH DAKOTA: *Examination*, Yankton, Dec. 6-7. *Endorsement*, Dec. 21. Sec., Dr. Gregg M. Evans, Yankton.

WASHINGTON: Seattle, Jan. 9-10. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WISCONSIN: Milwaukee, Dec. 7. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee.

Maryland June Report

Dr. John T. O'Mara, secretary, Board of Medical Examiners of the State of Maryland, reports the written examination for medical licensure held at Baltimore, June 18-21, 1940. The examination covered nine subjects and included ninety questions. An average of 75 per cent was required to pass. One hundred and forty-eight candidates were examined, 137 of whom passed and eleven failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1940)	84	82.1
George Washington University School of Medicine.....	(1939)	84	90.1
(1940) 78			
Georgetown University School of Medicine.....	(1933) 77,	(1939)	86
Howard University College of Medicine.....	(1938)		81
Rush Medical College.....	(1936)		82.1
Johns Hopkins University School of Medicine.....	(1939)		85
(1940) 79.2, 80.1, 81.1, 81.2, 81.4, 83, 83, 83, 83, 83,			
83, 83.3, 83.3, 84, 84.3, 85, 85, 85, 85, 85.2, 86,			
86.1, 86.2, 86.2, 87, 87, 88, 88, 88, 88.2, 89.4, 89.4,			
90, 90, 90.2, 92.1, 92.5			
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1940)	79.5	
80, 81, 81.4, 82, 82, 82, 82, 82, 82.2, 83, 83, 83,			
83, 83, 83, 83.1, 83.1, 83.2, 83.2, 83.4, 84, 84, 84,			
84.2, 84.3, 85, 85, 85, 85, 85, 85, 85, 85.1, 85.3,			
86, 86, 86, 86, 86.4, 86.4, 86.4, 87, 87, 87, 87.1,			
87.3, 87.5, 88, 88, 88.1, 88.3, 88.4, 89.1, 89.2, 89.4,			
89.4, 89.4, 90, 90, 90.1, 90.3, 91, 91, 91.3, 91.4, 92,			
92.1, 93			
Harvard Medical School.....	(1939)	86	
Tufts College Medical School.....	(1938)	81.4	
University of Minnesota Medical School.....	(1940)	89	
Columbia University College of Physicians and Surgeons.....	(1940)	91	
Cornell University Medical College.....	(1930)	87.5	
Hahnemann Med. College and Hospital of Philadelphia.....	(1938)	86	
University of Pennsylvania School of Medicine.....	(1938)	80.3	
83.2, (1940) 90.5			
University of Alberta Faculty of Medicine.....	(1940)	79.2	
Medizinische Fakultät der Universität Wien.....	(1930)	85	
Hamburgische Universität Medizinische Fakultät.....	(1924)	77.2	
Karl-Franzens-Universität Medizinische Fakultät, Graz.....	(1938)	83	
Universität Rostock Medizinische Fakultät.....	(1920)	79.3	
Magyar Királyi Erzsébet Tudományegyetem Orvostudományi, Pecs.....	(1926)	85.3	
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultása, Budapest.....	(1930)	76.5	
Universität Zürich Medizinische Fakultät.....	(1937)	81.4	
School	FAILED	Year Grad.	Number Failed
Hahnemann Medical College of Philadelphia.....	(1939)	1	
Karl-Franzens-Universität Medizinische Fakultät, Graz.....	(1922)	1	
Masarykova Universita Fakulta Lekarska, Brno.....	(1929)	1	
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin.....	(1926)	1	
Ludwig-Maximilians-Universität Medizinische Fakultät, München.....	(1906)	1	
Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau.....	(1926)	1	
Magyar Királyi Erzsébet Tudományegyetem Orvostudományi, Pecs.....	(1935)	1	
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultása, Budapest.....	(1930)	1	
Regia Università di Napoli Facoltà di Medicina e Chirurgia.....	(1923), (1934)	2	
Universität Basel Medizinische Fakultät.....	(1936)	1	

Twenty physicians were licensed to practice medicine by reciprocity and twelve physicians so licensed by endorsement from January 10 through July 31. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Georgetown University School of Medicine.....	(1932)	1932	New York
(1938) New Jersey			
Emory University School of Medicine.....	(1938)		Georgia
Johns Hopkins University School of Medicine.....	(1936)		Illinois
Creighton University School of Medicine.....	(1927)		Nebraska
University of Nebraska College of Medicine.....	(1937)		Nebraska
Columbia Univ. College of Physicians and Surgeons.....	(1931)		New York
Cornell University Medical College.....	(1938)		New York
New York Homeopathic Medical College and Flower Hospital.....	(1935, 2)		New York
Ohio State University College of Medicine.....	(1927)		Ohio
University of Oklahoma School of Medicine.....	(1935)		Oklahoma
Temple University School of Medicine.....	(1938)		Ohio
Woman's Medical College of Pennsylvania.....	(1937)		New York
Meharry Medical College.....	(1939)		Tennessee
University of Tennessee College of Medicine.....	(1935)		Louisiana

University of Tennessee Medical Department.....	(1890)	Alabama
Baylor University College of Medicine.....	(1939)	Texas
Medical College of Virginia	(1938)	N. Carolina, Virginia
School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
College of Medical Evangelists.....	(1936), (1937, 2),	(1938) N. B. M. Ex.
Yale University School of Medicine.....	(1935) N. B. M. Ex.	
Johns Hopkins Univ. School of Medicine.....	(1934), (1937, 2) N. B. M. Ex.	
Cornell University Medical College.....	(1936) N. B. M. Ex.	
University of Buffalo School.....	B. M. Ex.	
Duke University School of M.....	B. M. Ex.	

Book Notices

Handbook of Public Health Bacteriology and Chemistry: General Information Regarding Epidemiology, Collection and Shipment of Specimens, and Bacteriologic, Serologic and Chemical Procedures. Edited by M. S. Marshall, Department of Public Health, City and County of San Francisco, California. J. C. Geiger, Director. Second edition. Paper. Price, \$1.50. Pp. 150. San Francisco: J. W. Stacey, Inc., 1939.

The second edition of this useful manual retains the policy of brevity, conservatism and a careful selection of laboratory procedures. The consideration of epidemiology as a section has been omitted from this edition and epidemiologic points are considered in connection with each disease. The section on bacteriology of specific communicable diseases has been revised and discussions on chancroid, venereal lymphogranuloma and lobar pneumonia have been added. In the section on the bacteriology of shellfish the procedure of Dr. C. A. Perry of Baltimore is summarized. In the section on chemical procedures the phosphatase test for pasteurization is added. Notes on serology appear for the first time in the appendix. Other revisions and additions have been made without undue expansion of the manual. Every one engaged in public health work will find this condensed manual an invaluable and accessible source of practical information.

The Fundamentals of Nutrition. By Estelle E. E. Hawley, Ph.D., and Esther E. Maurer-Mast, M.D., University of Rochester School of Medicine and Dentistry, Rochester, New York. Including Table of 100-Calorie Portions. By Estelle E. Hawley, Esther E. Maurer and Herbert F. Van Epps, The Department of Vital Economics, University of Rochester, and Discussions of the Dietary Management in Specific Conditions. By Collaborators Associated or Formerly Associated with The University of Rochester School of Medicine and Dentistry. With a foreword by John R. Murlin, Ph.D., Sc.D., Professor of Physiology and Director of the Department of Vital Economics, University of Rochester. Cloth. Price, \$5. Pp. 477, with illustrations. Springfield, Illinois & Baltimore: Charles C. Thomas, 1940.

This book presents the subject of nutrition from a fresh point of view. Its contents are divided into five sections. The first section gives a brief but adequate discussion on energy metabolism and includes useful data and charts. The second section deals with the fundamentals of nutrition and includes three chapters, on classification of foods, calculation of energy requirement, the normal diet and low cost meals. Each chapter is concise, practical and down to date. Tables are used frequently to epitomize facts. The third section is devoted to diet therapy and includes discussions of the dietary management in specific disease by various physicians. The collaborators of this section are for the most part those associated with the University of Rochester School of Medicine and Dentistry and others who were formerly associated with the institution. These contributions are conservative in presentation and no attempt has been made to overemphasize the role of diet in the specific disease discussed. The discussions are short and to the point. The concluding chapter of this section is devoted to a discussion of vitamin and vitamin deficiencies. Each vitamin and the corresponding deficiency state resulting from its absence in adequate amounts are discussed in a clear and authoritative manner. The discussions are succinct and are presented in as practical a manner as possible. The fourth section is devoted to diet planning and includes a large amount of valuable and useful data. The authors have selected the 100 calory portion in preference to the 100 Gm. "share" or standard serving. They contend that the 100 calory portion establishes one common basis for comparison and in addition is easily visualized, since it is so frequently the average serving or simple multiple. These tables are useful and complete. The chapter on calculation of diets is clear and well done. Other chapters in this section include one

page discussions on the utilization of food and food exhibits. The concluding chapter provides the reader with some useful miscellaneous data that are not often found in the average textbook of nutrition. The fifth section is an appendix wherein one finds the most modern methods of evaluating the nutritional status of the patient, including vitamins. The chapter on commercial vitamin products is a practical and useful compilation of facts. The chapter on food hazards is well outlined. The concluding chapters are on recipes and food suggestions for special conditions and special diet instruction sheets. The bibliography after each chapter in the book is current and authoritative. The work is in reality a handbook which contains an adequate amount of epitomized descriptive material on each phase of nutrition. The authors have done an excellent job of editing and organizing. The material is conveniently presented in a concise, simple and practical manner. It is distinctly original and can be purchased with profit by those whose libraries are complete with textbooks on the subject of nutrition. The physician as well as the nutritionist and the dietitian will find the book most useful. It is an excellent reference work for the library of hospitals and medical schools on the subject of nutrition. Few textbooks on this subject contain such a wealth of facts and useful data.

Experimental Investigations in Serum Allergy with Reference to the Etiology of Rheumatic Joint Diseases. By Egon Bruun. Translated from Danish by Mrs. Clara Packness. Denne Afhandling er af det lægeriske Fakultet antaget til offentlig at forsvares for den medicinske Doktorgrad, København, 1939. Paper. Price, 24 Danish kroner. Pp. 229, with 49 illustrations. Copenhagen: Einar Munksgaard; London: Oxford University Press, 1940.

This book details the results of four years of research work in Copenhagen by Bruun, who attempted to corroborate the animal experiments of Klinge and others on "serum allergy" (inflammatory reactions in various tissues of animals sensitized to horse or other serum and treated with subsequent doses of the same serum). Of late a number of German and American workers have supported the hypothesis that allergy somehow takes part in the causation of chronic polyarthritis as well as rheumatic fever. Beginning in 1929, Klinge sensitized animals with subcutaneous injections of protein (fresh horse serum) and subsequently injected the antigen into knee joints of rabbits, producing in joints, heart, muscles, liver and other tissues lesions considered analogous to those of human "rheumatism." In the injected (but not in the noninjected) joints, acute phlegmonous and chronic nonsuppurative arthritis were produced; in heart muscle and valves, lesions appeared which included some resembling Aschoff bodies. The reactions varied in different animals depending largely on the number, size and timing of the subsequent doses of antigen. Not dismissing the role of bacteria in the production of human rheumatism, Klinge concluded that rheumatic joint diseases in man probably represent the reaction of allergically sensitive tissues to bacterial proteins.

Bruun has repeated and extended Klinge's experiments. Seventy-five rabbits were sensitized to sterile horse serum; then at varying periods they were subjected to one or more intra-articular injections of the same serum. With minor exceptions Bruun substantiated the results of Klinge. By varying the size, number and spacing of the injections he produced either an acute allergic inflammation (chiefly lymphocytic and not polymorphonuclear as in Klinge's cases) or a subchronic or chronic allergic inflammation not only in the injected joints but also in other tissues—heart, vessels, liver, spleen and muscles. In four animals allergic reactions were also found in the noninjected knee joint, producing what the author called "allergic polyarthritis." Giant cells of the foreign body and not of the Aschoff type participated in the myocardial reactions. In the uncomplicated experiments these inflammatory reactions were almost entirely "lymphohistiocytic" in type, but when short cold applications (ethyl chloride spray) were also applied to joints subjected to the injections of horse serum the resulting inflammation became largely polymorphonuclear, indicating that cold acted as a "parallergen."

Commenting on his results, the author discusses the role of the reticulo-endothelial system in allergic and immune reactions and sets forth the hypothesis that the large mononucleated or multinucleated, nonspecific, allergic macrophage giant cells, which

arise from normal resting histiocytes, proceed under specific influences to develop into different giant cell forms characteristic of the influence which provokes them. Thus, if an allergic giant cell is influenced by Koch's bacillus it will be converted into a giant cell of the Langerhans type; if the allergic macrophage giant cell is influenced by small tissue necrosis (such as may result from cold applications) there will probably appear a foreign body giant cell, and if it is influenced by streptococci there will probably appear an Aschoff giant cell.

In conclusion the author indicates a number of far reaching points of resemblance between sero-allergic tissue reactions in experimental animals and the pathologic changes encountered in rheumatic patients. Complete agreement between the results of experiments on serum allergy and human rheumatism cannot be expected, because in animal experiments nonbacterial allergy is purposely applied in order to determine the importance of the allergic factors, whereas in human beings it must be presumed that both the sensitizing and the provoking doses of antigen originate from bacteria. Although conclusive proof is not yet available, Bruun considers it probable that rheumatic joint diseases (that is, rheumatic fever and certain forms of polyarthritis) result from the action of bacteria (probably streptococci) in an allergically changed organism.

The report represents a great deal of careful painstaking work and should not be lightly regarded even by those who, in the current tradition, scoff at the widening application of "allergy." The author is obviously and somewhat annoyingly vague in his use of the terms "rheumatic diseases," "rheumatism" and "polyarthritis," but probably he is purposely vague as thereby he does not have to limit his vision prematurely. Since both myocardial lesions and chronic inflammatory lesions in joints (with pannus formation and partial ankylosis) were produced, the reader is permitted to infer that, if the author's hypothesis is valid, human rheumatic fever and chronic deforming polyarthritis may be rather closely related.

The author describes the technic used and the lesions produced in careful detail, perhaps in too much detail. There is a summary at the end of each of the five main chapters and another at the end of the book. Some condensation and less reiteration would have been possible without loss to clarity. The book is illustrated with excellent photomicrographs; had they been inserted in their appropriate and separate places rather than bound together toward the end of the book it would have been easier for the reader. About forty pages is given over to extracts from the animal necropsy records. A bibliography of 213 references is appended.

This study would have found a larger audience and been more readily available had it been published in an American or English medical journal devoted to experimental medicine or pathology. Those readers who will search for it in its present form will find it thought provoking and worthy of their serious consideration.

Surgery of the Hand: Wounds, Infections and Closed Trauma: A Book for the Practitioner and the Surgeon. By Marc Iselin, M.D., Surgeon, The American Hospital, Paris. Translated by T. M. J. d'Offay, M.B., Ch.B., F.R.C.S., Surgeon and Deputy Medical Superintendent, City General Hospital, Leicester, and Thomas B. Mouat, M.D., Ch.M., F.R.C.S., Surgeon, The Royal Infirmary, Sheffield, England. Cloth. Price, \$5.50. Pp. 353, with 135 illustrations. Philadelphia: Blakiston Company, 1940.

This translation brings to English and American students and practitioners Iselin's ideas on the treatment of injuries and infections of the hand and represents a serious attempt to raise the standards of treatment of injuries and infections of the hand. At the outset, in emphasizing the importance of the subject the author cites a number of cases of obviously neglected and badly treated cases. One wonders, however, whether French surgical practice is quite as casual and ill considered as one might conclude from the cases described. Chapters on tetanus and trophic and painful sequelae of hand injuries and a section on acute spreading infection have been added to the previous edition. The revised discussion of the treatment of wounds shows the marked influence of Böhler's teachings. The author's discussion of wounds loses some of its effectiveness in the manner of its presentation. Wounds due to aniline pencils, subungual hematoma, wounds with bone lesions and division of tendons are grouped in a single chapter

on wounds of the fingers, wounds of the thumb in another, and wounds of the hands in a third—divided into wounds of the thenar eminence, middle palmar region and so on. As a result of this confusion one has difficulty in obtaining a clearcut notion of the author's ideas concerning the proper treatment of uncomplicated injuries of soft tissues, tendon injuries or nerve division. Taken as a whole, this volume represents an unusually wide experience and serious interest in the subject of hand injuries and infections. It deserves whole hearted commendation.

Embalming Fluids: Their Historical Development and Formulation, from the Standpoint of the Chemical Aspects of the Scientific Art of Preserving Human Remains. By Simon Mendelsohn, F.A.I.C., Consulting Chemist, Cincinnati, Ohio. Cloth. Price, \$4. Pp. 166, with 8 illustrations. New York: Chemical Publishing Co., Inc., 1940.

The author has compiled an interesting and authoritative book, probably the first of its kind, for the practicing mortician. The subject matter includes a review of the historical development of embalming, some phases of the chemistry of putrefaction, the action, formulation and compounding of embalming fluids, the chemical and physical properties of preservatives, a few analytical methods, the determination of the phenol coefficient, a digest of jurisdictional regulations and a digest of American patents for embalming preparations. Some of the material has been obtained from antiquated and obsolete textbooks such as Barnes's *Art and Science of Embalming* (Chicago, 1905). An interesting section is that on the selective absorption of formaldehyde by different tissues, which has been taken from the master's thesis of G. M. Sleichter (University of Cincinnati, 1939). Much of the organic and analytical chemistry is beyond the scope of the average mortician. Physicians, especially pathologists; and public health workers would be interested in the data involving the preservation of bodies, the effect of chemicals on the bodies and the regulations in various states for the embalming and the transportation of bodies. The book is recommended to every practicing mortician, not for the purpose of having him prepare his own chemicals, but rather to give him a more complete understanding of the chemicals he uses.

Rheumatic Fever: Studies of the Epidemiology, Manifestations, Diagnosis, and Treatment of the Disease During the First Three Decades. By May G. Wilson, M.D., The New York Hospital and Department of Pediatrics, Cornell University Medical College, New York City. Cloth. Price, \$4.50. Pp. 595, with 79 illustrations. New York: Commonwealth Fund; London: Oxford University Press, 1940.

This is a record of the extensive experiences of the author with rheumatic fever and all its protean manifestations. Dr. Wilson has been a diligent student of this disease for more than twenty years and has had extensive and intimate clinical experience in heart clinics, wards and convalescent homes. The book is replete with observations and data that are seldom found in a textbook. While much of the material is distinctly original, the author has drawn on current contributions to enhance her discussions. The volume is organized into five parts and each part has a carefully selected bibliography. Part I is a brief but interesting historical survey of the subject and an excellent discussion of the epidemiology and etiology of the disease. Original investigations of Dr. Wilson and her collaborators relative to the etiology of rheumatic fever are recorded in some detail. Part II comprises a detailed discussion of the clinical and pathologic manifestations of rheumatic fever in childhood. The author presents numerous tables and graphic summaries to support and epitomize the text. Part III is a discussion of the course of the disease in the first three decades of life and concerns itself particularly with prognosis. As the basis for this discussion, 547 case records have been observed and critically analyzed. Her ingenious graphic presentation of data facilitates this presentation considerably. Part IV is a discussion of the diagnosis and functional classification of heart disease in children and part V is a discussion of the management of rheumatic fever with treatment and convalescent care receiving special emphasis. At the end of the book is a wealth of useful data arranged in tabular form on geographic incidence of the disease, epidemiologic and genetic analyses of rheumatic fever families, summaries of experimental protocols, technics of laboratory methods, values for red and white cells in children, blood pressure readings, Addis counts and special measures in nursing care and diets. While the author did not intend to write

a textbook or critical review of the subject, she has succeeded in presenting the reader with one of the most comprehensive and authoritatively documented discussions of the disease in print. The work reflects not only the painstaking and disciplined approach to the study of this disease but also a sound and critical evaluation of an immense amount of clinical and laboratory data. Dr. Wilson and her collaborators are to be congratulated for this contribution. It is a current source of facts about rheumatic fever in all its phases that should be eagerly sought by every practicing physician. This is a book that should be in every medical library.

Physiology of Micturition: Experimental and Clinical Studies With Suggestions as to Diagnosis and Treatment. By Orthello R. Langworthy, Lawrence C. Kolb and Lloyd G. Lewis. Cloth. Price, \$3.50. Pp. 232, with 49 illustrations. Baltimore: Williams & Wilkins Company, 1940.

After reviewing the anatomy of the bladder with particular reference to the nerve supply the authors present the evidence which has accrued during the past several decades with regard to the physiology of urination. The experimental work of others is discussed and the additional data which these collaborators have acquired from their own efforts is presented in detail. Throughout the text numerous illustrative case reports are given which include important cystometrographic evidence. Disturbances of urination of neurogenic origin are described in detail and theories as to the cause of the various symptoms presented by the particular type of case are advanced. A brief summary follows each chapter, emphasizing the important points which have been treated. This should serve as a valuable reference work for both advanced students and those urologists interested in learning more about the patient with obscure physiologic disturbance of the bladder mechanism.

Oral Surgery. By Sterling V. Mead, D.D.S., M.S., B.S., Second edition. Cloth. Price, \$12.50. Pp. 1,315, with 560 illustrations. St. Louis: C. V. Mosby Company, 1940.

This is the companion volume to Mead's *Diseases of the Mouth*, in which an attempt is made to treat oral disease from the surgical point of view. To this end the author discusses oral bacteriology, surgical technic, the sterile field, anatomic relations and other pertinent material. Adequate discussions are given of methods of extracting teeth, the treatment of fractures of the jaws, infections involving the mouth and neck and other items of interest in this field. One criticism may be directed toward this work, a defect which it shares in common with Mead's *Diseases of the Mouth*. The text is too long, it is too verbose and the author has an unhappy facility for complicating discussions of treatment with direct quotations from the current literature. This occupies an unnecessary amount of space, making the text unwieldy and difficult to read. Following each chapter is an extended bibliography, but many of the references cited are incorrectly spelled or misquoted. This careless handling of the bibliographic material greatly reduces the usefulness of the book for students. The volume is profusely illustrated with drawings and roentgenograms which are helpful. The book should be of interest to dentists, oral surgeons and others engaged in treating the diseases of the mouth and jaws.

Specific and Special Reactions for Use in Qualitative Analysis With Particular Reference to Spot Test Analysis. By F. Feigl, Ph.D., Consulting Chemist at the Research Laboratories for Fine-Chemicals, Nourypharma, Denver. Translated from a revision of the third German edition by Ralph E. Oesper, Ph.D., Professor of Analytical Chemistry at the University of Cincinnati, Cincinnati. Cloth. Price, \$3.50. Pp. 192. New York: Nordmann Publishing Company, Inc.; Amsterdam: Elsevier Publishing Company, Inc., 1940.

This is an excellent treatise on the theoretical considerations involved in the qualitative recognition of inorganic elements. The book is produced as a companion volume to the practical part by the same author, "Qualitative Analyse mit Hilfe von Tüpfelreaktionen," which has been translated into English. Likewise this work is an English translation of the third German edition together with some material from the forthcoming fourth German edition. This volume contains no technics utilized in qualitative analyses but discusses from a theoretical point of view the various factors affecting the sensitivity and specificity of reactions employed to recognize inorganic elements by the use of spot tests. Subjects such as types of complex chemical

compounds, masking of reactions, enhancement of reactivities, the effect of certain atomic groupings on specific activity and solubility, capillary phenomena and fluorescence analysis are taken up under chapter headings. To the student and teacher of qualitative micro-analysis this volume should be most welcome and helpful. Many suggestions can be obtained which will be of service in developing new tests—micro spot tests in nature—for the recognition of certain inorganic constituents in the presence of contaminants. Considerable discussion is given concerning organic complexes containing inorganic elements. This field is most promising not only qualitatively but also in quantitative analysis, as is manifest by the numerous quantitative technics now employing this behavior. The final chapter on fluorescence analysis gives many suggestions for further investigation. This is particularly fortunate, since this field promises to be quite fruitful to those interested in biometric assay problems. This book seems of value to the pure analyst rather than to the clinician or clinical pathologist. However, the toxicologist will find many useful theoretical considerations of spot tests which he may find advantageous. The volume contains an excellent bibliography and is free from typographic errors.

Standard Methods of the Division of Laboratories and Research of the New York State Department of Health. Augustus B. Wadsworth, M.D., Director. Second edition. Cloth. Price, \$7.50. Pp. 681, with illustrations. Baltimore: Williams & Wilkins Company, 1939.

The first edition of this work was widely accepted as a practical and dependable source of information on general and special technical laboratory procedures as used in the various branches of the Division of Laboratories of the New York State Department of Health. The second edition maintains this high standard with the addition of the new quantitative technic in the complement fixation tests, the revised colloidal gold test and new methods in the production, concentration and standardization of certain therapeutic serums. The book still remains one of the most current comprehensive and authoritative sources of information on laboratory methods in print and should be in the library of every health department laboratory and medical library.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Gastric Ulcer Allegedly Resulting from Burns.—In the course of his employment, May 8, 1937, Fickbohm, who was about 29 years old and in good health, washed a motor with kerosene. The kerosene ignited and Fickbohm suffered second degree burns of the forehead and arms, and third degree burns of the chest, face, ears, hands and shoulders. He received medical and hospital care and returned to work July 1, continuing at work until October 23. There was evidence, however, that during that period he was subject to fainting spells, that he coughed and spit up blood, that at various times he had to stay away from work and that his condition became progressively worse. On October 23 he quit work and went to Colorado to recuperate. On his return home again the following spring his condition seemed worse. April 2, 1938, he submitted to an operation, which revealed the fact that he was suffering from a perforated gastric ulcer. Four days later he died, the immediate cause of death, according to the attending physician, being diffuse peritonitis and bronchopneumonia. His legal heirs brought proceedings under the workmen's compensation act of Iowa to recover compensation for his death, basing their claim, apparently, on the theory that the burns received in the course of employment caused the ulcer and the peritonitis, which resulted in death. The district court, Woodbury County, Iowa, affirmed an award of compensation rendered by the industrial commissioner, and the employer and his insurance carrier appealed to the Supreme Court of Iowa.

From the expert testimony, said the Supreme Court, adduced at the hearing before the commissioner, it appears that gastric

ulcers as a result of external burns are of infrequent occurrence and do not often come to the attention even of experienced and busy practitioners. None of the physicians testifying at the trial, however, denied that this form of ulcer might follow external burns, although they stated that such a result occurred in only a small percentage of cases. Two physicians testified that in their opinion the probable cause of the ulcer and death was the burns, while four physicians were of a contrary opinion. The condition of the workman, as testified to both by lay witnesses and by the attending physician, exhibited symptoms which are those of an ulcer, and this fact was not disputed by any medical witness. There was evidence that when gastric ulcers are due to burns such burns create "a toxic condition which passes through the blood and affects the organs of the body." There was a contradiction in the expert testimony as to the time when such ulcers will develop, as well as to the ultimate fact—the cause of death. But from these contradictory opinions, continued the Supreme Court, and in consideration of all the testimony, the commissioner concluded that death was caused by the burns, in the course of and arising out of the employment. This finding, if based on disputed questions of material fact, was conclusive on this court.

The Supreme Court accordingly affirmed the award of compensation.—*Fickbohm v. Ryal Miller Chevrolet Co. (Ia.)*, 292 N. W. 801.

Medical Practice Acts: Pardon No Bar to Subsequent Proceedings to Revoke Physician's License.—In November 1929 the plaintiff, a licensed physician in the state of Florida, was convicted in a Florida court of perjury, possession of stolen goods and grand larceny and was sentenced to imprisonment in the state penitentiary for five years. In March 1933 he was granted a full and complete pardon for such offenses by the board of pardons of Florida. Subsequently the defendant, the state board of medical examiners of Florida, commenced proceedings to revoke the plaintiff's license to practice medicine on the ground that he had been convicted of a felony. The plaintiff thereupon petitioned the Supreme Court of Florida for a writ of prohibition to restrain the defendant from continuing the revocation proceedings. The board then filed a demurrer to the petition.

The plaintiff contended that his full and complete pardon constituted a complete defense to the revocation proceedings and deprived the board of all jurisdiction to conduct further hearings in the matter. The modern trend of authorities, said the Supreme Court, is that a pardon restores one to the customary civil rights ordinarily belonging to a citizen of the state, i. e., the right to hold office, to vote, to serve on a jury and to be a witness, but it does not restore offices forfeited nor property or interests vested in others in consequence of the conviction. Section 8495, Comp. Gen. Laws of Florida, 1927, specifically provides that a person receiving a full pardon shall be entitled to all the rights of citizenship enjoyed by him before his conviction. The rights of citizenship, however, do not include the right to practice medicine and, said the court, we have been unable to find a decision by a court of last resort holding that a full and complete pardon restores the extraordinary right to practice any of the professions. The privilege of pursuing the practice of a profession, continued the court, is based on the granting of a license by a sovereign state, which license is granted only to those possessing the necessary integrity and approved moral character. The power of the Florida legislature to require, as a condition precedent to the practice of medicine, that the practitioner not only be learned in his profession but possess qualifications of honor and good moral character cannot be questioned. Likewise, it was a proper exercise of its power for the legislature to provide for the revocation of the license of a practitioner of medicine who has been convicted of a felony in the courts of Florida. The adjudication of a medical practitioner's guilt of felony renders him a man of such character as to render it unsafe to trust the lives and health of the citizens of this state to his professional care. The doors of our homes should not be opened to receive men who hold themselves out as qualified medical practitioners when in truth and fact they have been convicted of crime. Therefore,

since the pardon in the instant case merely returned the plaintiff to the rights of citizenship which he previously had, and since those rights did not necessarily include the right to practice medicine, the court held that the effect of the pardon should not be construed or extended to abrogate the provisions of the medical practice act, requiring moral qualifications of medical practitioners, by restoring to the plaintiff a license which he was no longer morally qualified to retain. Accordingly, the court sustained the defendant's demurrer and denied the plaintiff's petition for a writ of prohibition.—*Page v. Watson et al. (Fla.)*, 192 So. 205.

Evidence: Admissibility of Results of Chemical Tests for Alcoholic Intoxication.—The defendant was prosecuted for operating a motor vehicle while under the influence of intoxicating liquor. Over the objection of the defendant, the trial court admitted in evidence the results of chemical analyses of the defendant's urine and blood which had been made to determine the quantity of alcohol, if any, in those body fluids. On the basis of this evidence the defendant was convicted of operating a motor vehicle while in an intoxicated condition, and he appealed to the Supreme Court of Iowa.

The defendant contended that the effect of the admission in evidence of the results of the chemical tests for alcoholic intoxication was to compel him to be a witness against himself in that he had been compelled to give the specimens of blood and urine against his will. This contention, however, did not meet with the approval of the Supreme Court. Although the circumstances under which the specimens of blood and urine were obtained were not described in the published report, the court held that there was no evidence whatever of either compulsion or entrapment. In fact, said the court, the evidence showed that the defendant voluntarily gave the specimens in the hope that the results obtained by analysis would demonstrate that he was not intoxicated and thus free him from the charge brought against him. Accordingly, the judgment of conviction was affirmed.—*State v. Morkrid (Iowa)*, 286 N. W. 412.

Workmen's Compensation Acts: Student Nurse an Employee.—In the opinion of the Supreme Court of Wisconsin, a student nurse who pays the hospital where she is to receive her training a nominal entrance fee and a determined amount for books and uniforms to be used during the training period, who must render certain services to the hospital during that period and who is furnished board, room and laundry by the hospital is an employee of the hospital. An injury to such a student nurse arising out of and in the course of such employment, consequently, is compensable under the workmen's compensation act of Wisconsin.—*Employers Mut. Liability Ins. Co. v. Industrial Commission (Wis.)*, 292 N. W. 878.

Society Proceedings

COMING MEETINGS

- American Society of Anesthetists, New York, Dec. 12. Dr. Paul M. Wood, 745 Fifth Ave., New York, Secretary.
- American Student Health Association, Ann Arbor, Mich., Dec. 27-28. Dr. Ralph I. Canuteson, University of Kansas, Lawrence, Kan., Secretary.
- Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.
- Puerto Rico, Medical Association of, San Juan, Dec. 13-15. Dr. David E. Garcia, P. O. Box 3866, Santurce, Secretary.
- Radiological Society of North America, Cleveland, Dec. 2-6. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
- Society of American Bacteriologists, St. Louis, Dec. 27-29. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
- Southern Section, American Laryngological, Rhinological and Otological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.
- Southern Surgical Association, Hot Springs, Va., Dec. 10-12. Dr. E. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
- Western Surgical Association, Topeka, Kan., Dec. 6-7. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

200:429-576 (Oct.) 1940. Partial Index

- Medical and Social Approaches to the Problem of Chronic Rheumatism. R. B. Osgood, Boston.—p. 429.
- "Target Cell" Anemia: Anerythroblastic Type of Cooley's Erythroblastic Anemia. W. Dameshek, Boston.—p. 445.
- Anemia and Water Retention. M. B. Strauss and H. J. Fox, Boston.—p. 454.
- Failure to Control Polycythemia Rubra Vera with Lipocain and Choline. G. Carpenter, Chicago.—p. 462.
- Blood Pressure Determinations by Patients with Essential Hypertension: 1. Difference Between Clinic and Home Readings Before Treatment. D. Ayman and A. D. Goldshine, Boston.—p. 465.
- Delayed Electrocardiographic Changes in Coronary Occlusion. S. Strauss, Chicago.—p. 474.
- Cardiac and Respiratory Function at Rest in Patients with Uncomplicated Polycythemia Vera. M. D. Altschule, Marie C. Volk and H. Henstell, Boston.—p. 478.
- Manometric Determination of Effects of Various Sulfanilamide Compounds on Brucella Melitensis. W. Kemper, B. Wise and C. Schlager, Durham, N. C.—p. 484.
- Penetration of Blood Clot by Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfamethylthiazole. C. N. Duncan and J. M. Faulkner, Boston.—p. 492.
- Thrombocytopenic Purpura Due to Sulfapyridine. H. K. Russell, White Plains, N. Y., and R. C. Page, New York.—p. 495.
- Postpubertal Menorrhagia and Its Possible Relations to Thrombocytopenic Purpura Haemorrhagica. H. L. Goldburgh and B. A. Gouley, Philadelphia.—p. 499.
- *Acute Nephritis: Review of Seventy-Seven Cases. J. M. Hayman Jr. and J. W. Martin Jr., Cleveland.—p. 505.
- Evaluation of Brucella Opsonocytaphag Test. B. Wise, Durham, N. C.—p. 520.
- Intubation Studies of Human Small Intestine. W. G. Karr, W. O. Abbott, Olive D. Hoffman and T. G. Miller, Philadelphia.—p. 524.
- *Clinically Associated Deficiency Diseases. T. D. Spies, A. P. Swain and Jean M. Grant, Cincinnati.—p. 536.
- Vitamin C in Epilepsy: Dilantin Sodium Not a Cause of Vitamin C Deficiency. H. H. Merritt and Althea Foster, Boston.—p. 541.

Acute Nephritis.—Hayman and Martin maintain that the conception of acute glomerular nephritis as a disease of children which follows severe infections, especially scarlet fever, and is characterized by albuminuria, hematuria, edema and convulsions has been shown to be inadequate. While acute nephritis is more common in children than in adults, it may occur at any age. Moreover, not only is the prognosis more serious in the older age groups but the onset is frequently more insidious and the symptoms less dramatic. The authors describe the symptoms and clinical course of seventy-seven cases of acute glomerular nephritis treated in Lakeside Hospital from 1931 to 1939. All age groups were represented. A history of preceding infection was obtained in seventy-five of seventy-seven cases. Infection of the upper respiratory tract, sinuses and ears accounted for fifty-six (75 per cent). While the disease occurs at all ages, it is most common before 30. The cardinal symptoms of hematuria, hypertension and edema were not all present in every case. Evidence of cardiac involvement was present in approximately half the cases. Ten patients died in the hospital, seven (9 per cent) primarily of acute nephritis. Fifty-two of the remaining sixty-seven patients were followed for from six months to eight years. Of these thirty-five (67.3 per cent) are well, nine (17.3 per cent) have persistent albuminuria or hypertension, while three have died of uremia since discharge from the hospital, and five have chronic glomerular nephritis.

Clinically Associated Deficiency Diseases.—Spies and his associates report observations on 1,250 malnourished persons. The subjects were selected from persons presenting themselves for examination either at the Hillman Hospital, Birmingham, Ala., or the General Hospital, Cincinnati. The patients made frequent visits to the clinic, during which they

were weighed and examined. Diagnosis of a specific deficiency state was based on the presence of symptoms characteristic of it. Thus diagnosis of pellagra was made only if characteristic mucous membrane lesions, dermal lesions or both were present; diagnosis of riboflavin deficiency depended on the presence of characteristic angular lesions of the mouth, or ocular symptoms; diagnosis of beriberi was made only in the presence of nutritional neuritis. The diagnosis in each instance was confirmed by the response of the patient to the specific therapeutic agent administered under controlled conditions. In general, the method of confirmation consisted in the dramatic response to the administration of synthetic nicotinic acid or its compounds, synthetic riboflavin, synthetic thiamine hydrochloride or synthetic vitamin B₆, the patient's diet remaining constant. Many of these patients had other diseases, such as scurvy, which was treated with synthetic ascorbic acid, and vitamin A deficiency, which responded to carotene or oleum percomorphum. That many of these persons must suffer from general malnutrition even though they have no symptoms of a specific deficiency disease is indicated by an analysis of the dietaries of fifty cases which shows that they are deficient to some extent in each of the essential nutrients. These patients have mixed rather than single deficiency disease, and months and years of ill health precede the diagnostic lesions of a specific deficiency. The authors believe that the confusion regarding vitamins or deficiency diseases is partly due to the discovery that vitamin B, formerly considered a single substance, is composed of twelve or more separate factors, each, together with unknown substances, contributing to the total effect of therapeutic agents such as yeast, wheat germ or liver extract. Although the administration of a single chemical substance was followed by a response of the lesion for which it was specific and by a great increase in the patients' strength, the improvement in general was greater when they were given a number of synthetic materials than when they were given any one alone. Furthermore, when supplements of dried brewers' yeast powder or liver extract were given in addition to synthetic materials to persons who continued to eat their usual inadequate diets, there was an even greater improvement in their general health.

American J. Obstetrics and Gynecology, St. Louis

40:361-544 (Sept.) 1940. Partial Index

- Retrodiscalplacement of Uterus in Relation to Pregnancy, with Special Reference to Technic and End Results of Bissell Operation. A. H. Aldridge, New York.—p. 361.
- Method for Evaluating Stress of Urinary Incontinence. A. C. Barnes, Ann Arbor, Mich.—p. 381.
- Uterine Bleeding Induced by Progesterone: During Normal Menstrual Interval and in Amenorrhea. B. Zondek, Jerusalem, Palestine; S. Rozin and M. Vesell, New York.—p. 391.
- Calcium, Phosphorus and Nitrogen Metabolism in Women During Second Half of Pregnancy and Early Lactation. F. W. Oberst, Lexington, Ky., and E. D. Plass, Iowa City.—p. 399.
- Effect of Vitamin K Administered to Patients in Labor. J. E. Fitzgerald and Augusta Webster, Chicago.—p. 413.
- *Coincidence of Tuberculosis of Endometrium with Tuberculosis of Lung. J. E. Lackner, W. Schiller and A. S. Tulskey, Chicago.—p. 429.
- *Pelvic Tuberculosis: Report of Case of Tuberculosis of Cervix. A. H. Lahmann and S. F. Schwartz, Milwaukee.—p. 439.
- Clinical Study of Effects of Diethylstilbestrol on Puerperal Women. H. F. Connally Jr., D. I. Dann, J. M. Reese and L. H. Douglass, Baltimore.—p. 445.
- Intra-Uterine Onset of Hemorrhagic Disease of Newborn. C. T. Javert, New York.—p. 453.
- Studies on Preservation of Placental Blood. J. Scudder, C. R. Drew and V. G. Damon, New York.—p. 461.
- Effect of Salt Poor Diet During Pregnancy on Duration of Labor. W. Pomerance and I. Daichman, Brooklyn.—p. 463.
- Acute Intestinal Obstruction Complicating Pregnancy and Postpartum Period: Report of Four Cases. F. Weintraub and B. Jaffe, Brooklyn.—p. 481.
- Velamentous Insertion of Umbilical Cord: Cause of Fetal Death in a Twin Pregnancy. J. W. Records, Oklahoma City.—p. 504.
- Paraldehyde Analgesia and Perineal Anesthesia in Obstetrics. C. K. Fraser and J. W. Jones, Durham, N. C.—p. 506.
- Bilateral Fibroma of Ovaries Combined with Degenerating Adenoma of Right Breast. Eva Haumeder, New Hampton, Iowa.—p. 514.
- Viable Triplets Delivered by Cesarean Section. L. Smith and D. Cathcart, Atlanta, Ga.—p. 515.

Coincidence of Tuberculosis of Endometrium and Lung.—Lackner and his associates studied the endometrium of 125 women suffering from pulmonary tuberculosis. Clinically two groups of tuberculous endometritis can be distinguished. The first is involvement associated with progressive

tuberculosis of the ovaries, the tubes or both. The endometritis represents only an associated pathologic process of minor clinical importance. The second is tuberculosis of the endometrium with normal tubes and ovaries, associated with and developing from a tuberculous infection of an organ outside the pelvis, such as the lungs and lymph nodes. This represents an important and obviously unsuspected syndrome of primary extragenital tuberculosis. It is in the latter group that the authors tried to determine how often women with primary progressive tuberculosis of the lungs would show an isolated clinically latent tuberculosis of the endometrium. Only women with evident progressive tuberculosis of the lungs, with no clinically manifest inflammatory process of the ovary or tube, were examined. Only two cases of manifest primary endometrial tuberculosis were found among the 125 women. The history and clinical observations of these two cases are meager and resemble that of most of the cases of tuberculous endometritis gleaned from the literature. Both patients apparently had normal or almost normal menstrual cycles. They had no gynecologic complaints. Vaginal examination was negative in one case and it elicited minimal changes in the other case. The incidence of two cases among 125 harmonizes with the figures obtained from the necropsy records of the Cook County Hospital during the last ten years. The incidence in the necropsy material was 1.87 per cent as compared with 1.6 per cent in the clinical material. The authors use Ghon's classification. In the first type with endogenous spread a generalized infection, with the local tuberculosis representing only a part of the generalized infection, must be distinguished from an isolated hematogenic focus or metastasis. The second type of endometrial tuberculosis represents "reinfection" and is represented by cases of a new infection in some other organ after a primary focus has developed in one organ. The two cases reported are classified as isolated metastasis of a primary pulmonary process. By exclusion the hematogenic route must be accepted as the method of spread. It may be similar to the spread of miliary tuberculosis, the difference being that the circulating tubercle bacilli found the endometrium the only favorable nidus. An example of this type of secondary tuberculosis is hematogenic salpingitis. The authors believe that the occurrence of an isolated hematogenic tuberculous endometritis would appear to be proved by the observations in their two cases.

Pelvic Tuberculosis.—Lahmann and Schwartz believe that tuberculous involvement of the female genitalia is more prevalent than is generally assumed. It has been estimated as constituting from 5 to 8 per cent of all pelvic inflammatory conditions and therefore should be considered in the differential diagnosis of any disorder of the female genitalia. Symptoms and signs are not typical and resemble those of many other maladies affecting the genitalia. Genital tuberculosis is usually secondary to tuberculosis elsewhere in the body and occurs most frequently during active sexual life. There is a marked tendency for the disease to descend from the tubes to the endometrium, involving the tubes in 90 per cent, endometrium in 75 per cent, ovaries in 30 per cent, cervix in 5.5 per cent and vagina and vulva in 0.5 per cent. There is no tendency for the disease to spread to the urinary tract. During a period of eleven years twenty-one women with tuberculosis involving the genitalia were admitted and treated at the Milwaukee County General Hospital. Positive evidence for the diagnosis could not be obtained in six instances as no tissue was available for microscopic study, and these have been excluded from discussion. Twelve of the fifteen were between 20 and 30 years of age. The oldest patient was 43. Not even in one instance was the diagnosis of genital tuberculosis correctly made or even considered preoperatively. In only one case was the diagnosis made by the operating surgeon. Symptoms of tuberculosis of the female genitalia resemble those of chronic gonorrheal salpingitis. The two most common complaints were pain in the lower part of the abdomen confined to one or both sides, and vaginal discharge, usually of long standing. Other symptoms in their order of frequency were loss of weight, urinary distress, vomiting, weakness, cough, abdominal mass, fever and chills. Eight patients are alive and well, including one on whom a right salpingo-oophorectomy

was performed in 1930 when the patient was 27 years old. Four patients could not be located and the remaining three are known to be dead. There was a high incidence of immediate postoperative complications. The most serious of these was draining sinuses from the incision, many fecal in character and of long standing. Sinuses which drained from approximately four months to four years developed in eight patients. Six of the surgical incisions healed primarily. Pelvic tuberculosis, according to the authors, may be spread by (1) contiguity, from the soft tissues adjoining the pelvis, (2) lymphogenically, usually from the abdominal cavity, (3) hematogenically, from some distant focus and (4) primarily, with direct inoculation by coitus. The only case of tuberculosis of the cervix (probably primary) that was encountered is cited. Pulmonary involvement was encountered in 20 per cent of the patients.

Anesthesiology, New York

1:121-240 (Sept.) 1940

- Water Exchanges Due to Anesthetic Drugs. H. G. Barbour, New Haven, Conn.—p. 121.
 *Bronchopneumonia: Anesthetist's Responsibility? R. M. Waters, Madison, Wis.—p. 136.
 Intravenous Anesthesia. J. S. Lundy and R. C. Adams, Rochester, Minn.—p. 145.
 Effect of Various Tissues on Detoxification of Evipal in Dog. S. J. Martin, H. C. Herrlich and B. B. Clark, Albany, N. Y.—p. 153.
 Production of Ventricular Tachycardia by Adrenalin in Cyclopropane Anesthesia. C. R. Allen, J. W. Stutzman and W. J. Meek, Madison, Wis.—p. 158.
 Laboratory Studies on Prophylaxis and Treatment of Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia. C. L. Burstein, B. A. Marangoni, A. C. DeGraff and E. A. Rovenstine, New York.—p. 167.
 Oxygen Therapy and Resuscitation. E. H. Warnock and R. M. Tovell, Hartford, Conn.—p. 187.
 Duration of Local Anesthesia in Relation to Concentrations of Procaine and Epinephrine. A. J. Leser, Los Angeles.—p. 205.
 *Hyperthermia Following Anesthesia: Consideration of Control of Body Temperature During Anesthesia. G. E. Burford, New York.—p. 208.
 Endotracheal Nitrous Oxide Anesthesia for Tonsillectomy: Report of 1,550 Cases. K. C. McCarthy, Toledo, Ohio.—p. 216.

Bronchopneumonia.—Waters believes that with rare exceptions pulmonary morbidity follows a period of interference with normal respiration whether due to drugs, trauma or illness. Many of the signs and symptoms seen in patients depressed by illness or trauma are also observed as side effects of drugs administered to relieve pain. Illness, injury and pain therapy may interfere with normal breathing by interfering with the normal innervation, psychic activity, muscle tone, activity of the respiratory center and inhaled atmospheres. Improvement in the incidence of pulmonary morbidity lies along the line of preventing these complications and not in the treatment of bronchopneumonia after it is established. So far the occasional occurrence before, during and after anesthesia of a period of interference with normal respiration has not been prevented. Patients are still encountered who after operation, after sedative and narcotic drug administration, after head injuries or even during debilitating illness have atelectasis, massive collapse, bronchopneumonia and other major respiratory disease. Delay in the care of abnormally functioning respiration is fatal. Changes in pulse rate, respiration, blood pressures and body temperature afford earlier evidence of the onset of trouble than do cyanosis and auscultatory or percussion evidence. Such changes can be masked by oxygen therapy. Careful inspection of the respiratory movements viewed from the foot of the bed, laterally and from the head may make evident the asymmetry which is the cardinal sign of atelectasis. Similar management has been useful for prophylaxis and therapy. All markedly depressed patients should be treated by the "stir-up regimen." This means the hourly insistence on making the patient take several deep breaths and cough effectively, and changing his position radically. Active aid and encouragement by the attendant is required. Frequently a depressed patient with inactive breathing and inefficient or absent cough can be made to expel large quantities of secretion from the air passages. One may cause the unconscious or completely uncooperative patient to take several deep breaths by pouring pure carbon dioxide from a rubber tube held over the face. Such a flow of gas added to the inspired air may force the desired ventilation of inactive alveoli. Carbon dioxide is of therapeutic value for this specific purpose. When there is the slightest evidence of obstruction or of atelec-

tasis, tracheobronchial toilet, aspiration of secretions, is justified. This apparently drastic regimen, when instituted early and faithfully, has reduced the incidence of major respiratory complications and has reduced the severity of many of those still encountered. Markedly depressed breathing must be made adequate either manually or mechanically. Carbon dioxide therapy is not a physiologic remedy for depressed breathing. Oxygen therapy is logical for only half of the picture and may require supplemental augmentation of respiratory exchange to restore normal conditions.

Hyperthermia Following Anesthesia.—Burford encountered three instances of excessive hyperthermia in children following ether anesthesia during hot weather. Frequent records of temperature taken during anesthesia showed numerous moderate but unimportant elevations. They indicate that ether anesthesia, contrary to the opinion widely held, does not lower body temperature. These frequent moderate elevations and the cases of high temperatures suggest that under propitious conditions the factors working toward disturbance of thermal control during anesthesia become accentuated. The rise in temperature to around 108 F. is accompanied by a remarkable elevation of pulse and respiratory rates. One of the author's cases terminated in death. The condition is probably due to the simultaneous disturbance of heat production, heat loss and integration of the activities of the central nervous system related to temperature regulation. The adequate integration of these complex processes between heat production and heat loss requires continuous control by the central nervous system. The control of this diverse activity is centered in the hypothalamus. Abnormalities of heat regulation develop subsequent to lesions at the base of the brain involving the hypothalamus. Specific subdivisions of the hypothalamus control separately heat production and heat distribution. In hot weather, dispersion of heat is accomplished with difficulty, especially in children. Radiation and convection from the skin ordinarily account for the largest part of heat loss. On hot humid days, when the atmospheric temperature approaches the body temperature, the effectiveness of these mechanisms is curtailed. Vaporization from the skin then becomes the chief means of cooling the body. Vaporization during anesthesia meets certain man made impediments. As a result of complete draping during operation, convection and radiation are made more difficult and vaporization can become effective only after perspiration has moistened at least two layers of overlying sheets. The perspiration of a small child may not be sufficient to accomplish this. Vaporization from the skin of the face and from the lungs is impaired by the anesthetic mask and the anesthetist's arm. The administration of ether is associated with a marked adrenergic response, and the internally secreted epinephrine increases tissue metabolism and heat production. Secretion of the thyroid may also be increased through an ultimate effect of an original adrenergic response. This total effect on elevation of temperature achieves significance only through the coexisting impairment of heat distribution. Added to this, the control of the central nervous system on heat regulation may be faulty. Heat regulation in infants and small children is notoriously erratic. This may be related to the immature development of the central nervous system or of certain of its tracts. The three mechanisms of heat control can become affected in the course of anesthesia. The elevated rate of combustion of tissue is possibly aided by struggling during induction. The small rise of temperature is uncompensated. For each rise of 1 degree F. in body temperature, an increase of 7 per cent in the basal metabolic rate occurs. This adds to the production of heat which is already uncompensated. Thus a vicious cycle is established: increased heat causing increased metabolism and increased metabolism producing increased heat. This continues until the cycle is broken. Otherwise high temperatures are attained that produce either permanent damage to the central nervous system or death. The author studied the incidence and direction of changes in temperature of fifty patients during operations performed during the winter under various anesthetic agents and lasting three fourths of an hour or more. There were thirty-three elevations of temperature. Twenty of the elevations were probably no greater than those that normally develop in normal

individuals not under anesthesia; however, the five elevations of from 2 to 3 degrees F. are well beyond the normal range. In twenty the rise was less than 1 degree F. and in eight it was from 1 to 1.8 degrees F. Excessive hyperthermia occurs rarely enough to cause great concern, but when infants and children are scheduled for prolonged operations under ether anesthesia during hot weather the possibility of its development should be considered, and axillary temperatures made a part of the anesthesia record might provide a timely warning.

Annals of Internal Medicine, Lancaster, Pa.

14:361-564 (Sept.) 1940

- Observations on Effect of Coramine in Certain Cardiac States. W. D. Stroud and P. H. Twaddle, Philadelphia.—p. 361.
Iron Metabolism and Its Relationship to Anemia and Therapy. W. M. Fowler and Adelaide P. Barer, Iowa City.—p. 378.
*Bronchostenosis Complicating Allergic and Infectious Asthma. L. E. Prickman and H. J. Moersch, Rochester, Minn.—p. 387.
*Pharmacologic Treatment in Schizophrenic Patients. S. Katzenelbogen, A. Simon, Anna R. Coyne, C. Vigue and R. Cohn, Washington, D. C.—p. 393.
Anticatalase Activity of Sulfanilamide and Sulfapyridine in Vivo. M. Clyman, Philadelphia.—p. 406.
*Blood Pressure Studies on University Students, Including Effect of Exercise on Essential Hypertension, Hypotension and Normal Subjects. E. A. Thacker, New Orleans.—p. 415.
Treatment of Illness of Emotional Origin by the Internist. E. Weiss, Philadelphia.—p. 424.
Hematologic Aspects of Space Consuming Lesions of Bone Marrow (Myelophthisic Anemia). S. R. Mettler, San Francisco.—p. 436.
Erythema Multiforme Exsudativum (Hebra): Clinical Entity Associated with Systemic Features. H. Keil, New York.—p. 449.
New Observation Helpful in Diagnosis of Coronary Thrombosis. P. J. Steiner, Hartford, Conn.—p. 495.
Living with the Weather. F. M. Potenger, Monrovia, Calif.—p. 502.

Bronchostenosis Complicating Asthma.—Prickman and Moersch believe that bronchostenosis, a definitely localized stricture-like narrowing of a bronchus, is more common than is generally observed. Bronchostenosis is primarily inflammatory and is not referable to allergic edema or bronchial spasm. The lesion inhibits the movement of air entering or leaving the segment of pulmonary tissue beyond the stenosis and retains bronchial secretions below the stenosis, so that an area of partial or complete atelectasis results. Among 140 patients suffering from asthma, examined with the bronchoscope, sixty were found to have definite stenosis of one or more bronchi. A study of these patients showed that bronchostenosis complicating asthma generally produces characteristic symptoms and, frequently, physical and x-ray signs. One prominent symptom is severe, persistent and sometimes paroxysmal cough. At first it is impossible for the patient to raise sputum and when it appears it is profuse, usually mucopurulent and in 40 per cent of the cases is at some time streaked with blood. The severe coughing is apparently caused by the patient's attempt to raise secretions retained by the stenotic area and later, when the stenosis recedes (spontaneously or because of bronchoscopic dilatation) the retained secretions are more easily raised. The sputum is probably blood tinged because of the bronchial inflammation and secondary pulmonary congestion which is present. Febrile episodes, either with or without preceding chills, occurred in 68 per cent of the cases. The fever is explained by the toxicity from the retained secretions and the inflammation. Febrile episodes, hemoptysis or purulent sputum do not accompany uncomplicated asthma and therefore the presence or history of any one of these features in asthma should suggest bronchostenosis or some other organic complication. Of the sixty patients, 53 per cent gave a history of pneumonia and 35 per cent of pleurisy. Bronchostenosis is frequently mistaken for bronchopneumonia. Roentgenograms of the thorax may show an area of pneumonitis or atelectasis. After the acute phase subsides, bronchoscopic examination reveals a stenosed bronchus and dilatation by forceps introduced through the bronchoscope, and aspiration of the retained secretion usually relieves it. An adult or a child who has asthma and who experiences one attack or repeated attacks of "pneumonia" should be suspected of having had stenosis of a bronchus until proved otherwise. The physical signs which may accompany bronchostenosis are secondary to the atelectasis. They consist of suppression of breath sounds and fremitus over the affected area and dulness to percussion over the atelectasis. In uncomplicated asthma physical signs are equal in each lung. The x-ray observations of bronchostenosis are

usually those characteristic of atelectasis or, less frequently, bronchiectasis. Only a few patients with asthma require bronchoscopy, but it should be done as it will rule out or confirm the presence of bronchostenosis. In addition to bronchostenosis caused by localized inflammation, bronchostenosis referable to malignant changes complicating allergic asthma, as was found in one of the sixty cases, tuberculosis or ulceration of calcareous material may be possible. Almost every case of bronchostenosis complicating asthma may be traced to an acute infection of the respiratory tract. Postural drainage is important when bronchial secretions are in excess. Daily postural drainage will help to correct the stagnation of secretions that apparently contributes to the development and aid in preventing recurrences of bronchostenosis. In half of the authors' patients the asthma had an allergic basis. The immediate results (relief of the patient, subsidence of fever, reduction in amount and improvement in character of the sputum, improvement of the asthma and often immediate reversal of physical signs of bronchial obstruction) of dilation and aspiration are excellent.

Pharmacologic Treatment of Schizophrenia.—Katzenelbogen and his colleagues present their experience with the following aspects of insulin shock therapy of schizophrenia: sensitivity to insulin, reactions following individual injections, unusual reactions (hazards) during and following individual treatments, biochemical studies, electro-encephalographic studies and therapeutic results. 1. Both men and animals may be hyposensitive or hypersensitive to insulin. The amounts necessary to provoke shock or hypoglycemic reactions varied from 25 to 400 units. Tolerance to insulin may change throughout the treatment. 2. The most common vegetative system reactions, profuse perspiration and abundant salivation, are usually simultaneous. The cardiovascular system responds with marked fluctuations in the pulse rate. The respiratory system usually does not show significant changes in the precoma phase of the treatment, but in the comatose state irregular, stertorous and deep heavy breathing is frequent. The body temperature more often than not goes down. General muscular relaxation or rigidity is frequent before and during the comatose state. Abolition of the corneal reflexes, weakening of the plantar reflexes or marked extension of the big toe are common during coma. The most dramatic reactions are excitement, motor restlessness, clonic convulsions and drowsiness. Usually each patient reacts along the same pattern throughout the treatments, but the quality, intensity, sequence and duration of the reactions may vary in different patients and in the same patient on different days. 3. Eight of the authors' 140 patients had unusual reactions: cardiovascular collapse, prolonged deep coma, apnea and cyanosis. Only one of these patients died. 4. Biochemical studies show that of the thirty-two variables analyzed in blood before the administration of insulin and during coma some showed changes during therapy beyond normal fluctuation and errors of the methods. Serum solids showed a tendency to increase, while the other blood constituents showed a definite decrease and then a trend toward the original level. Sugar and fermentable sugar diminish considerably and remain at a low level throughout the individual treatments. The blood sugar and inorganic phosphorus curves do not keep pace throughout treatment, the sugar curve remains low and the phosphorus rises gradually to the original level and in some cases above that level. The relationship between the hypoglycemia, the reactions and the dose of insulin are not qualitatively or quantitatively consistent. 5. The fifty brain action potentials studies in seventeen schizophrenic patients revealed two distinct types of "brain waves." In the first (in forty-two records) a fairly normal alpha rhythm, from eight to ten cycles per second, predominated during the earlier interval of recording. This was followed by a gradually steady decrease as the hypoglycemia progressed. Within a few hours of insulin injection a low frequency brain wave pattern averaging three cycles per second became predominant. There was a striking parallelism between the variations in the brain potentials and the changes in the blood sugar content. With intravenous dextrose the brain wave pattern often returned to its original preinsulin type within ten minutes; with gavage the return was longer but did not exceed thirty minutes. 6. Thirty-five of the patients were completely free from psychotic symptoms and made satisfactory adjustment

outside the hospital. Twenty-five patients were improved to the extent that there was a markedly favorable change in their behavior, with satisfactory social adjustment in the hospital and under certain favorable circumstances outside the hospital. The remaining patients showed no change. Twenty-four of the patients with remissions had been affected one year or less.

Blood Pressure Studies of University Students.—Thacker studied blood pressure records of 15,000 male university students and tried to ascertain the effect of exercise on them from a comparative standpoint. A systolic blood pressure over 150 mm. of mercury on entrance was considered hypertensive and one below 108 hypotensive. Exercise tests were not performed by students with discernible organic heart, kidney or thyroid disease. The same type of exercise, consisting of raising the weight of the body twenty times from the floor on to a chair 18½ inches high at the rate of forty cycles per minute, was performed by all subjects. The comparative effect of exercise was studied on the ninety-six hypertensive, fifty-six hypotensive and 128 normal subjects on whom the cold pressor test had been conducted for vasomotor response. The systolic blood pressure of 20 per cent of the hypertensive students increased more than 60 mm. of mercury and in 2 per cent the increase was more than 80 mm. The systolic pressure in the normal group failed to increase more than 50 mm. in 82.7 per cent and in none did it rise more than 60 mm. In the low blood pressure group, 91.6 per cent failed to show an increase of more than 30 mm. and none more than 40 mm. The average increase of the systolic pressure was respectively 48, 37 and 23 mm. of mercury for the hypertensive, normal and hypotensive classes. The diastolic pressure decreased in all three groups; more than 91 per cent of the normal and hypotensive students and 79 per cent of the hypertensive subjects did not have more than a 10 to 20 mm. decrease. Only about 8.5 per cent of the normal and low pressure groups had a diastolic decrease of 21 to 30 mm. as compared to 18.7 per cent of the hypertensive subjects. Following exercise the systolic pressure of the normal group returned to the basal level within five minutes as compared to only 78.8 per cent of the high pressure group and 74.8 per cent of the low pressure group. The pulse rate following exercise of the normal and low pressure cases returned to the basal level within two minutes; the average for the hypertensive cases was three and one half minutes. The average pulse rate increase after exercise was respectively thirty, thirty-four and thirty beats per minute for the high, normal and low pressure groups. The increase in the blood pressure cannot be attributed to this factor alone, as in many subjects a marked increase in the systolic blood pressure existed with only a slight increase in the pulse rate, and vice versa. The maximal average systolic pressure after exercise in the hypertensive group rose 30 mm. above the ceiling reached when the cold test was used. The regular or usual systolic blood pressure in the hypertensive class was 28 mm. above the basal level as compared to 5 and 7 mm. in the low and normal groups. From a detailed history of the students it was observed that 11.7 per cent of the normal, 14.3 per cent of the low pressure and 43.7 per cent of the hypertensive groups presented evidence of being nervous or easily excited. Also 3.1 per cent of the normal and 5.3 per cent of the low blood pressure and 54.1 per cent of the hypertensive groups gave a history of familial hypertensive cardiovascular disease. Likewise 17.8 per cent of the hypotensive class gave a family history of low blood pressure, whereas none of the high blood pressure and only 2.3 per cent of the normal subjects indicated such a familial disturbance. Perhaps the definite hereditary pattern for blood pressure depends for the most part on some structural or physiologic phenomenon of the autonomic nervous system and/or endocrine function, which are passed through the germ plasma. Of the students in the high pressure group 35.4 per cent were heavy eaters, as compared to 14.8 and 14.3 per cent of the normal and low pressure subjects. The history of the amount of exercise or work done appears to be of little importance as a causative factor in the production of essential hypertension. The fallacy of one blood pressure test is revealed by the fact that 64.8 per cent of the students with a systolic pressure above 150 mm. at the time of their entrance physical examination had normal pressures at the first recheck, as were 82.2 per cent of the hypotensive subjects.

Archives of Pathology, Chicago

30:843-992 (Oct.) 1940

- Changes in Number of Circulating Leukocytes in Relation to Spontaneous Recovery from Pneumococcal Infection: Experimental Animal Used, Guinea Pig. M. S. Fleisher and G. T. Rich, St. Louis.—p. 843.
- Atherosclerosis: II. Lipids of Serum and Tissues in Experimental Atherosclerosis of Rabbits. S. Weinhouse and E. F. Hirsch, Chicago.—p. 856.
- Phagocytosis of Collagen. G. A. Vassos Jr., New York.—p. 868.
- Specificity of Fetal and Adult Human Hemoglobin Precipitins. Ruth Renter Darrow, Sophie Nowakovsky and Margaret Howard Austin, Chicago.—p. 873.
- Microscopic Structure of Striated Muscle in Heat Rigor: Nodal Multiplication of Striae. E. J. Carey, Milwaukee.—p. 881.
- Mitosis in Specimens Removed During Day and Night from Carcinoma of Large Intestine. W. B. Dublin, R. O. Gregg and A. C. Broders, Rochester, Minn.—p. 893.
- Chemotaxis of Monocytes Contrasted with That of Polymorphonuclear Leukocytes and Lymphocytes. D. R. Coman, Philadelphia.—p. 896.
- Intravital Staining of Malignant Neoplasms in Man by Evans Blue. A. Brunschwig, R. L. Schmitz and T. H. Clarke, Chicago.—p. 902.
- Does Chronic Irritation Cause Primary Carcinoma of Human Lung? Madge Thurlow Macklin and C. C. Macklin, London, Ont.—p. 924.

Journal Industrial Hygiene & Toxicology, Baltimore

22:253-302 (Sept.) 1940

- Hydrogen Cyanide Gas Fumigation. J. E. O'Donnell, H. W. Mundt, W. N. Knudsen and P. H. Delano, Fort Peck, Mont.—p. 253.
- Settling Characteristics of Various Inorganic Dusts. L. H. Berkelhamer, Saranac Lake, N. Y.—p. 276.
- Acute Response of Guinea Pigs and Rats to Inhalation of Vapors of Tetra-Ethyl Orthosilicate (Ethyl Silicate). H. F. Smyth Jr. and Jane Seaton, Pittsburgh.—p. 288.
- Dermatitis Venenata Resulting from Contact with Aqueous Solution of Ethyl Mercury Phosphate. F. J. Vintinner, Concord, N. H.—p. 297.

New England Journal of Medicine, Boston

223:481-522 (Sept. 26) 1940

- Treatment of Prostatic Obstruction. R. M. Nesbit, Ann Arbor, Mich.—p. 481.
- Football: Review of Injuries in Boston Secondary Schools. J. H. Burnett, Boston.—p. 486.
- *Treatment of Sydenham's Chorea by Fever and Vitamin B Therapy. S. Stone, Manchester, N. H.—p. 489.
- Treatment of Pneumonia. M. Finland, Boston.—p. 499.

Fever and Vitamin B for Chorea Minor.—In view of the frequency of cardiac changes in chorea and the fear of untoward complications following eight hours' exposure of a child to a temperature of 104 F. or over, as recommended by Neymann, Stone reduced the fever time and increased the number of treatments. The factor of vitamin B deficiency was considered as a possible contributing cause in the development of cardiac involvement and the hyperirritability of the nervous system. The patient's diet was therefore complemented by the addition of vitamin B complex given orally, and in some cases by thiamine hydrochloride given intravenously. In the last three years the author has treated twenty children suffering from chorea. Seven patients exhibited all the signs of severe chorea, as manifested in continuous movement of the face and extremities, inability to feed or dress themselves, hypotonia and muscle weakness, and inability to walk without support. The other thirteen patients presented moderately severe or mild forms of the disease. A number of patients gave a history of an attack of severe chorea from three months to two years previously, from which they had apparently never completely recovered. The author's method of treatment for severe cases (an advanced cardiac condition was not found to be a contraindication to the treatment) consisted in giving the patient six or seven fever treatments, one every three or four days, and maintaining the temperature at 104 F. or over for about two hours. Every treatment was followed by the injection of from 10 to 15 mg. of thiamine hydrochloride intravenously shortly after removal from the fever cabinet, while the temperature still remained elevated. The patients received from 4 to 8 cc. of vitamin B complex orally three times daily. Recovery was produced with about fourteen hours of fever at 104 F. or over. When this was combined with vitamin B therapy, advanced cardiac conditions were found to be no contraindication to the fever treatment. Usually a change for the better in the carditis was noted at the end of the treatment. One of the two patients treated with thiamine hydrochloride responded with cessation of symptoms after the second intravenous injection of 10 mg. of the drug. Various degrees of behavior disturbances were seen in most of the moderately severe and milder cases. They all received from 4 to 8 cc. of vitamin B complex orally,

three times a day. The improvement in physical manifestations was less rapid than it was in the fever-treated patients, but most of the symptoms disappeared within one month. No hospitalization was required for any patient in this group. Improvement was noted in their behavior concomitantly with the change for the better in the choreic manifestations.

New Orleans Medical and Surgical Journal

93:111-168 (Sept.) 1940

- Problem of Prostatism. M. H. Foster, Alexandria.—p. 111.
- Management of Chronic Prostatitis. C. O. Frederick, Lake Charles.—p. 115.
- Treatment of Hyperplasia of Prostate with Diethylstilbestrol and Diethylstilbestrol Dipropionate: Preliminary Report. P. J. Kahle and E. Maltry, New Orleans.—p. 121.
- Pulmonary Tuberculosis: Pathology and Pathogenesis. E. L. Burns, New Orleans.—p. 131.
- Id.: Early Diagnosis from the Standpoint of the Pediatrician. E. Naef, New Orleans.—p. 136.
- Id.: Early Diagnosis. M. W. Miller, New Orleans.—p. 139.
- Studies with Antigens: V. Analysis of Comparative Skin Reactions by Means of the Chi Square Statistic. M. R. Pabst, C. H. Boatner and B. G. Efron, New Orleans.—p. 142.
- Medical Societies of Louisiana Prior to the War Between the States. W. D. Postell, New Orleans.—p. 150.

Public Health Reports, Washington, D. C.

55:1707-1758 (Sept. 20) 1940

- *Rheumatic Heart Disease in Philadelphia Hospitals: Study of 4,653 Cases of Rheumatic Heart Disease, Rheumatic Fever, Sydenham's Chorea and Subacute Bacterial Endocarditis Involving 5,921 Admissions to Philadelphia Hospitals from Jan. 1, 1930, to Dec. 31, 1934: III. Fatal Rheumatic Heart Disease and Subacute Bacterial Endocarditis. O. F. Hedley.—p. 1707.

Rheumatic Heart Disease in Philadelphia Hospitals.—According to Hedley, of 4,653 cases (5,921 admissions) of rheumatic heart disease, rheumatic fever, Sydenham's chorea and subacute bacterial endocarditis admitted to Philadelphia hospitals from Jan. 1, 1930, to Dec. 31, 1934, 21.9 per cent ended fatally. If subacute bacterial endocarditis apparently not superimposed on rheumatic heart disease is excluded there were 916 deaths, or 20.2 per cent, among the 4,538 cases. Of 3,445 cases of rheumatic heart disease, excluding all subacute bacterial endocarditis, 732, or 21.3 per cent, terminated in death. Subacute bacterial endocarditis apparently not engrafted on rheumatic heart disease was the cause of death in 104, and of the 916 fatal cases of rheumatic heart disease 901 were due primarily to rheumatic heart disease including deaths from subacute bacterial endocarditis when occurring as a complicating factor. The causes of the other fifteen deaths were due to various causes, including empyema, traffic accidents, operations and diabetes, but had this study been based on postmortem examinations rather than clinical observations this percentage of 1.6 would probably have been substantially increased. With one possible exception, in no instance was death attributable to the arthritic manifestations of rheumatic fever or the cerebral manifestations of Sydenham's chorea. The mean age at death from rheumatic heart disease, regardless of its association with subacute bacterial endocarditis, was slightly less than 30 years. The proportion of deaths from rheumatic heart disease in hospitals among Negroes was not as great as might be expected. This is probably influenced by the age distribution of the Negro population as a result of recent migration. Among the 916 deaths more than 63 per cent occurred during the 10 to 19, 20 to 29 and 30 to 39 decades; more than 50 per cent of deaths occurred among persons less than 30 years of age, while only 3 per cent occurred among persons more than 60 years of age. The studies do not suggest that deaths from rheumatic heart disease in Philadelphia hospitals are more common among foreign born persons or among persons of foreign extraction than among old stock white Americans; if anything, the opposite obtains. This is probably influenced by the readiness with which various racial groups avail themselves of hospital facilities, their economic status and the relative age of foreign groups dependent on the period of greatest immigration. Fatalities from rheumatic heart disease were disproportionately high among the laboring classes. There were few deaths among professional men. As the disease develops during childhood, persons with rheumatic heart disease are not as likely to engage in occupations requiring strenuous exertion as the social status of the laboring classes would suggest. Rheumatic heart disease causes approximately 200 deaths annually in Philadelphia hospitals;

165 are due primarily to rheumatic heart disease, while thirty-five are due to subacute bacterial endocarditis superimposed on rheumatic heart disease. In about 0.1 per cent of hospital admissions for all causes, death is due to rheumatic heart disease. The mean age at onset was 14.7 years, the mode 9.3 years. The mean interval between the primary manifestation and death was 13.4 years. Among 542 fatal cases in which the duration from onset to death was ascertained, death resulted in less than one year in 13.5 per cent, in less than five years in nearly 32 per cent and in less than ten years in more than 48 per cent. At least from 3.5 to 4.5 per cent of first attacks terminated fatally. This percentage becomes higher if deaths from fulminating rheumatic carditis without arthritic manifestations of rheumatic fever are included. Despite the preeminence of Philadelphia as a medical center, the problem is a local one as at least 87.2 per cent of fatal cases were among residents. The mean annual death rate from rheumatic heart disease in hospitals among Jewish persons was approximately the same as among Gentiles. Of 116 pregnant women with rheumatic heart disease, 18.1 per cent died.

Southern Medical Journal, Birmingham, Ala.

33:1015-1116 (Oct.) 1940. Partial Index

- Hysterectomy:** Review of 1,000 Consecutive Hysterectomies at St. Anthony Hospital, Oklahoma City. W. Long, W. B. Poole, Oklahoma City, and T. J. Hardman, Tulsa, Okla.—p. 1015.
- Indications and Contraindications for Cesarean Section.** J. E. Kanatser, Wichita Falls, Texas.—p. 1023.
- Radiation Therapy in Treatment of Metastatic Malignancy of Chest.** R. G. Giles, San Antonio, Texas.—p. 1033.
- Common Vesicular Lesions of Hands and Feet: Diagnosis and Treatment.** C. B. Kennedy, New Orleans.—p. 1036.
- Treatment of Severe Staphylococcal Infections with Sulfapyridine and Its Sodium Salt.** W. B. Martin and R. B. Grinnan Jr., Norfolk, Va.—p. 1039.
- The Genesis of Pellagra.** S. Harris, Birmingham, Ala.—p. 1044.
- Some Uses of Vitamin B₁ in Neurology and Psychiatry.** J. A. Willie, Oklahoma City.—p. 1056.
- Effects of Foods and Drugs on Cataracts.** T. W. Moore, Huntington, W. Va.—p. 1060.
- *Night Blindness and Vitamin A Deficiency in Pulmonary Tuberculosis.** R. Harris and J. S. Harter, Jackson, Miss.—p. 1064.
- Follow-Up on Craniofacial Injuries.** J. Greenwood Jr., Houston, Texas.—p. 1077.
- Treatment of Chronic Urticaria: Based on Successful Outcome of Seventeen Out of Eighteen Cases.** I. S. Kahn and Emma M. Grothaus, San Antonio, Texas.—p. 1086.
- Influence on Public Health Progress of Inadequate Medical Services in the Rural Population.** C. B. Crittenden and Lois Skaggs, Louisville, Ky.—p. 1092.
- Similar Fibroid Tumors Occurring in Identical Twins.** G. Walsh and R. M. Pool, Fairfield, Ala.—p. 1098.
- Standardization of Medical Schools: Origin and Present Day Application of the Program.** F. C. Zapffe, Chicago.—p. 1100.

Night Blindness, Vitamin A Deficiency and Tuberculosis.—Harris and Harter studied the photometer readings of 114 ambulant institutional patients with pulmonary tuberculosis. The tests showed about an equal deficiency in vitamin A in the few newly admitted patients so studied. The diet in this institution has been carefully worked out and contains everything necessary to a point of luxury. The minimal reading of 0.6 was regarded as normal, from 0.6 to 2 as pathologically borderline and more than 2 millifoot candles as unmistakably pathologic. Of the patients tested, fifty were pathologic at the first test, sixty-one were borderline and three were normal. At the end of one week each patient having had 30,000 units of halibut liver oil daily, of thirteen pathologic cases tested eight were still pathologic and five borderline. At the end of three weeks, on the same dosage, nineteen of the originally pathologic patients were tested: four were still pathologic and fifteen fell in the borderline class. Of twenty-five originally pathologic patients tested after having been on 30,000 vitamin A units of halibut liver oil for two months, three were normal and twenty-two were high borderline. At the end of five months, of fourteen tested five were normal and nine very high borderline. Thirty-five of the originally pathologic patients were discharged before the end of five months. The author concludes that marked vitamin A deficiency in any individual might indicate that a thorough chest examination is in order if no other cause is found for the deficiency. Large doses of halibut liver oil may be necessary. Fifty and more years ago pulmonary tuberculosis was treated with cod liver oil and the physicians of that time were positive that it helped. Vitamin A in large doses may offer a worthwhile treatment in ocular tuberculosis.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

52:233-288 (Aug.-Sept.) 1940

- Notes on Scleroderma (Dermatomyositis).** T. Lewis.—p. 233.
- Generalized Scleroderma.** G. B. Dowling.—p. 242.

British Journal of Ophthalmology, London

24:421-468 (Sept.) 1940

- Some Observations on Present Position of Our Knowledge of Intra-Ocular Fluid.** S. Duke-Elder, J. C. Quilliam and H. Davson.—p. 421.
- Experiments on Effect of Ascorbic Acid in Mustard Gas Burns of Eye.** Ida Mann and B. D. Pullinger.—p. 444.
- Boeck's Sarcoidosis of Lacrimal Gland.** H. B. Stallard.—p. 451.
- Chronic Granuloma of Lacrimal Sac: Case.** H. B. Stallard.—p. 457.

British Journal of Urology, London

12:161-220 (Sept.) 1940

- Injuries of Kidney.** R. H. J. Swan.—p. 161.
- Injuries of Bladder.** A. R. Thompson.—p. 177.

British Medical Journal, London

2:373-404 (Sept. 21) 1940

- *Spontaneous Hyperventilation Tetany.** F. S. Fowweather, C. L. Davidson and L. Ellis.—p. 373.
- Insulin Treatment of Pulmonary Tuberculosis.** G. Day.—p. 376.
- Lead Encephalopathy Simulating Cerebral Tumor.** A. M. Nussey and I. Drybrough-Smith.—p. 379.
- *Sulfanilamide as Preservative in Stored Blood.** R. F. Hunwicke.—p. 380.
- The War as an Etiologic Factor in Psychiatric Conditions.** W. S. Maclay and E. Guttmann.—p. 381.

Spontaneous Hyperventilation Tetany.—Fowweather and his co-workers have encountered five cases of spontaneous hyperventilation tetany. The serum calcium was determined as a routine measure in each of them and in four the serum inorganic phosphorus. In three the phosphorus was in the neighborhood of 1 mg. per hundred cubic centimeters of serum. The authors believe this figure to be much lower than previously reported in this type of case. The results in these three cases are so definitely below the normal range as to be of valuable diagnostic significance, making phosphorus determination a useful addition to the methods of diagnosis. The specimens of blood were taken immediately after an attack. The serum calcium in four of the cases was at a high normal level, while in the fifth it definitely exceeded the normal. The three patients whose blood was examined when they were free from attacks gave figures below those obtained just after an attack. The first three patients had attacks of tetany during the course of another illness, which may well have been a contributing factor in the production of the tetany or a precipitating cause of the attacks. Spasmodic attacks were the major complaint of the other two patients. Both patients were obviously of neurotic type—one "full of complaints" and the other giving a history of hysterical fits. To the authors the most probable explanation of spontaneous hyperventilation tetany appears to be as follows: As a result of certain stimuli—physical or emotional—some individuals respond by overbreathing. If this is sufficient to reduce the carbon dioxide concentration in the blood, alkalosis will follow and in its turn may be sufficient to cause an attack of tetany. The attack is mainly due to tissue alkalosis and ends spontaneously, largely as a result of the tendency to tissue acidosis consequent on the muscular activity of the tetany itself. Cessation of overbreathing also occurs and assists in the return to normal conditions. The principal factor is the tendency to overbreathe among those of emotionally unstable temperament, sufferers from anxiety neuroses and the like. The tendency may be influenced by physical factors. Other factors which probably play some part are the state of the acid-base equilibrium when the overbreathing takes place and the susceptibility of the subject to alkalosis and its effects. Conditions other than tetany which have been associated with hyperventilation have been described under the terms "neurocirculatory asthenia" and "effort syndrome." Therefore alkalosis resulting from spontaneous hyperventilation may cause either tetany or the conditions referred to. What determines the actual clinical manifestations in any given case is not apparent. However, (1) effort syndrome and related conditions without tetany are

rarely, if ever, seen as a result of voluntary overbreathing in normal individuals, (2) in spontaneous tetany resulting from hyperventilation and sometimes in the tetany induced by voluntary overbreathing in normal persons many of the symptoms (breathlessness, dizziness, faintness, palpitation, tremor) associated with effort syndrome and the like are also present but tend to be overshadowed by the tetanic spasms and (3) in cases of spontaneous hyperventilation tetany, effort syndrome and the like there is a background of anxiety, emotional stress or other psychologic disturbance.

Sulfanilamide as Preservative for Stored Blood.—Hunwicke confirms the experiments of Novak that sulfanilamide in comparatively low concentrations has a preservative effect on blood stored at refrigerator temperatures. Novak recommends the addition of 20 mg. of sulfanilamide to 100 cc. of blood. In one of the experiments reported by Hunwicke this did not prove adequate. The use of higher concentrations, say up to 1:1,000, would seem to offer a solution of the problem, provided the initial contamination is negligible. When complete sterility is achieved there is no need for any addition to the blood, but this is a rare condition as usually there are a few organisms present which do not reveal themselves until the blood has been in the refrigerator for some days or weeks, when they begin to multiply. It is to guard against wastage of blood and the possible consequent danger of heavy contamination that the addition of sulfanilamide is suggested. The sulfanilamide must be added to the blood in concentrated sterile solution. The solution when added to the blood must be still warm, that is before crystallization begins.

South African Medical Journal, Cape Town

14:291-310 (Aug. 10) 1940

The Epileptic and His Treatment. M. J. Cohen.—p. 293.
Radiologic Signs of Gastroduodenal Ulcers. S. Ferreira.—p. 294.

Chinese Medical Journal, Peiping

58:1-140 (July) 1940

Studies on Mechanism of Insulin Convulsions: I. Significance of Serum Electrolytes; II. Effects of Breathing Atmospheres Varying Widely in Oxygen and Carbon Dioxide Content. I. McQuarrie, M. R. Ziegler and W. E. Stone.—p. 1.
Id.: Effects of Varying Partial Pressures of Atmospheric Oxygen and Carbon Dioxide in Adrenalectomized Animals. I. McQuarrie, M. R. Ziegler, W. E. Stone, O. H. Wangenstein and C. Dennis.—p. 26.
*Immunization Against Whooping Cough: I. Controlled Study of Prophylactic Vaccination in an Orphanage. F. T. Chu and J. P. Wu.—p. 39.
Metabolic Studies on Roasted Soybean Meal as Infant Food. C. Fan, Theresa T. Woo and F. T. Chu.—p. 53.
Acute Encephalitis in Children: Clinical and Serologic Study of Ten Epidemic Cases. F. T. Chu, J. P. Wu and C. H. Teng.—p. 68.
Involvement of Nervous System in Mumps. I. Snapper.—p. 79.
Muscular Dysfunction in Glycogen Storage Disease. C. Fan and Theresa T. Woo.—p. 88.
Note on White Blood Cell Counts in Whooping Cough. C. T. Ch'in.—p. 98.
Growth and Development of Chinese Infants of Hunan Province: I. Body Weight, Standing Height and Sitting Height During First Year of Life. T. F. Su and C. J. Liang.—p. 104.
Tuberculosis in Children in Shanghai. C. L. Kao.—p. 113.

Immunization Against Whooping Cough.—Chu and Wu observed the effect of active immunization of thirteen children against whooping cough during an epidemic in a local orphanage. The thirteen children were inoculated at weekly intervals for three weeks with vaccine prepared from phase I organisms. About five months after the completion of the vaccination of these thirteen children whooping cough appeared at the institution. Facilities for the isolation of the orphanage children were entirely lacking. Of the thirteen children vaccinated prior to the outbreak none developed the disease in spite of continuous and prolonged exposure. On the other hand typical pertussis developed in twenty-three, or 67.6 per cent, of thirty-four non-vaccinated children whose age, mode of living and degree of exposure were the same as those of the vaccinated children. The serum agglutinin titer for *Haemophilus pertussis* increased during the course of the epidemic in seven of the vaccinated children, indicating clearly that they had been exposed. The remaining six vaccinated children likewise showed increased agglutinin titers, but they had been given an additional dose of vaccine during the early part of the epidemic. The authors are convinced of the effectiveness of the method for preventing pertussis.

Note e Riviste de Psichiatria, Pesaro

69:115-244 (April-June) 1940

*New Prophylaxis Against "Protracted Coma" in Insulin Shock Therapy. F. Accornero and A. Giordani.—p. 115.
Treatment of Colibacillary Psychoses. D. de Rosa.—p. 149.
Homosexuality. A. Cucchi.—p. 173.
Mechanism of Convulsant Action of Acetylcholine Intravenously Administered. A. Rossi.—p. 183.
Clinico-Anatomic Observations of a Case of Alzheimer-Perusini Disease. G. Fattovich and Cecilia Cavagna.—p. 209.

Prevention of Prolonged Coma in Insulin Shock Therapy.—Accornero and Giordani report the successful use of 1-phenol-2-methylaminopropanol in preventing prolonged coma in eleven selected cases of dementia praecox (six of which were of the paranoid type) after insulin shock treatments. The drug, added to the sugar solution and administered by means of a stomach tube in doses varying from 6 to 12 mg., was able to reduce coma to periods varying from ten to twenty-five minutes in patients who previously had been observed to require fifty minutes and even six and a half hours to recover consciousness. Though given daily for as long as two months in high doses, the drug was well tolerated and elicited no untoward effects. Their three year experience with the drug proved that it had to be given in combination with the sugar solution. Delayed administration not only lowered efficacy but tended to negative results. The authors point out that in no case was prolonged shock due to overdosage with insulin. Prolonged shock, they believe, is likely to occur even when all precautions have been observed because of the variability of effect of the same dosage in the same person on successive days due to hypoglycemic fluctuation or to retarded absorption of the carbohydrates under the influence of excessive acidity of the gastric juice. They recommend that the drug be used to prevent prolonged coma in persons known to have a tendency to revive slowly rather than that it be relied on as a means to interrupt protracted coma after it has already set in.

Lisboa Médica, Lisbon

17:423-480 (July) 1940. Partial Index

*Identification of *Trichomonas vaginalis* in Leukorrhoeas. A. B. Corrêa Mendes.—p. 432.
Waterhouse-Friderichsen's Syndrome: Case. Silva Nunes.—p. 459.

Trichomonas vaginalis in Leukorrhoea.—Corrêa Mendes made a comparative study of stained dried smears of either fresh or dry vaginal secretions and microscopic preparations of fresh vaginal secretions of 120 women with leukorrhoea. Microscopic preparations were made with the vaginal secretion in physiologic solution of sodium chloride. The smears were prepared by the "roll film" method, allowed to dry, fixed by heat and stained by Jensen's modification of Grams method. The results of the two methods agreed in 116 cases, there being thirty-five positive results for *Trichomonas* and eighty-one negative results. In four cases *Trichomonas* was identified by the dried staining method alone, after failure of fresh microscopic preparations. The author believes that the methods of stained dried smears and of microscopic preparations of fresh vaginal secretion have the same diagnostic value in identifying *Trichomonas vaginalis*. The practical value of the smear method is greater than that of preparations of fresh secretion. Bacteria other than *Trichomonas* may be identified. In cases of *Trichomonas* infection reported by the author, the vaginal secretion did not contain Döderlein's bacilli. The vaginal bacterial flora corresponded to that of the third degree of Cruickshank and Sharman's classification. Control of protozoal infection resulted in a modification of the bacterial flora to the type which corresponds to the first degree of Cruickshank and Sharman's classification. *Trichomonas* was present in association with gonorrhea in three cases, with eumycetes in two and with spiriles in three cases. The vaginal secretion of twelve pregnant women contained eumycetes alone or in association with vibrios in the absence of *Trichomonas*. *Trichomonas* is identified in dried stained smears by the appearance of the protoplasm and by the position of the nucleus and the presence of stained flagella. The protoplasm is granular and foamy. The nucleus appears as an elongated mass uniformly stained red in the proximal end of the protozoon near the point of insertion of flagella, which usually, though not necessarily, takes the red stain.

Zeitschrift für Tuberkulose, Leipzig

85:1-64 (June) 1940

- *Special Apparatus for Endoscopic Examination of Tuberculous Patients and for Intracavernous Aspiration Technic According to Monaldi. J. Abelló.—p. 1.
Suction Drainage in Treatment of Residual Caverns. W. Kremer.—p. 11.
Cure of Congenital Giant Cyst of Lung. H. Brügger.—p. 14.
Extensive X-Ray Shadows in Children with Tuberculosis. Hanna Fischer.—p. 18.
The Tuberculous Patient at Work. E. Brandt.—p. 24.

Endoscopic Examination and Monaldi's Intravenous Aspiration.—Abelló, in discussing the technic of Monaldi's intracavernous aspiration (see abstract in THE JOURNAL March 9, 1940, p. 934) and the instruments used for this procedure, describes an instrument developed by him which enables one to inspect the interior of a cavity. The basic idea of the instrument is the use of the thoracoscope in connection with the Monaldi method. He designates his instrument as a cavernoscope or pleurothoracoscope. The instrument has the diameter of a No. 12 Nelaton catheter. The upper end of the lamp is constructed like Bottari's trocar and thus the thoracoscope can serve as a trocar. The instrument is introduced with the lamp lighted. In order to prevent the prism becoming clouded at the time it enters the cavity it is passed over an alcohol flame. The apparatus can also be used to close the drainage bronchi by means of diathermy. The author gives detailed description of the practical application of his method. Following roentgenologic localization of the cavity a Saugman needle is introduced at the most favorable point. The trocarthoracoscope is then introduced by the same course as the needle. Following inspection of the cavity, the cavernoscope is withdrawn and replaced by a rubber tube. The cavity should be entered, if possible, 2 or 3 cm. above the base, for if it is entered near the base it becomes easily stopped up. The position of the tube must be controlled by x-ray examination. Since coughing may cause misplacement or even expulsion of the tube, it should be attached to the wall of the thorax. The author advises twenty-four hours of rest before aspiration is begun.

Sovetskaya Meditsina, Moscow

Pp. 1-52 (Nos. 13-14) 1940. Partial Index

- More Data on Curative Value of Conserved Tissue. V. P. Filatov.—p. 5.
Treatment of Gunshot Wounds. B. E. Linberg.—p. 8.
Wounds of the Lung and Pleura. M. A. Arjev.—p. 11.
Treatment of Suppurating Wounds with Cold Quartz Lamp. D. K. Yazykov.—p. 14.
Methyl Violet Therapy of Burns. D. M. Rapoport.—p. 15.
*Procaine Hydrochloride Block of Vishnevsky for Spontaneous Gangrene and Trophic Ulcers. L. M. Shnaper.—p. 26.
*Nicotinic Acid Therapy in Pellagra of Children. P. S. Gershenovich, A. M. Maksudov and Ts. G. Ioffe.—p. 29.

Spontaneous Gangrene and Trophic Ulcers.—Shnaper treated fifteen cases of spontaneous gangrene of the extremities, twelve cases with trophic ulcers, two cases with circulatory disturbances due to chilblain and one case due to a snake bite. The patients with spontaneous gangrene complained of excruciating pain in the extremity, intermittent claudication, coolness and cyanosis of the extremity with the development of gangrene of the toes or the entire extremity. As a rule there was no pulsation in the dorsal pedal artery and in some of the cases in the popliteal. All the patients had been previously submitted to a number of medical and surgical procedures without success. The treatment consisted of a circular procaine hydrochloride block according to the method developed by Vishnevsky. From 200 to 225 cc. of a 0.25 per cent of procaine hydrochloride solution was slowly injected into the skin and subcutaneous tissue and below the aponeurosis in a circular fashion above the lesion. This procedure was followed by a mild rise in temperature, normal sleep and disappearance of pain within the first twenty-four hours. The pain returned after this period but was much less intense and disappeared gradually in from two to five days. The affected extremity became warmer and a line of demarcation rapidly developed in cases exhibiting beginning gangrene of toes or fingers. In some of the cases the circular block was supplemented within three weeks by a lumbar block (injection of from 75 to 100 cc. of procaine hydrochloride solution into the right or left lumbar region). The favorable effect was observed for periods of from one and one half to two years.

The rationale of the treatment is based on Speransky's theory that local irritation involves the central nervous system with the resulting upset in the normal internervous relations. He proposed the method of treating trophic lesions by interrupting the conduction of painful reflexes.

Nicotinic Acid Therapy in Pellagra of Children.—Gershenovich and his associates treated children with pellagra of the ages from 1 to 13 years in the pediatric clinic of Tashkent. The severe cases of pellagra presented clinical manifestations on the part of the skin, the gastrointestinal tract, the tongue and the nervous and psychic spheres. Children with subclinical pellagra presented diarrhea, lasting from two to six months and not yielding to ordinary dietetic therapy, marked dystrophy, asthenia, dryness of the skin and disturbances of pigmentation. The greater majority of the cases presented characteristic pellagrous glossitis with redness and erosions. The advanced pellagrins appeared emaciated, asthenic and apathetic and suffered from severe diarrhea and total anorexia. Nicotinic acid was administered intramuscularly in a 1 per cent solution in distilled water in doses of 1 cc. for a child aged 1 year, 2 cc. for a child aged 2 years, 3 cc. for a child aged 3 years, 4 cc. for a child aged 4 years, 5 cc. for children of ages from 5 to 10 years and from 6 to 8 cc. for children above that age. The injections were given daily, in some cases twice a day. From ten to fifteen injections were necessary to accomplish a cure. Among the accompanying reactions the authors noted hyperemia of the tongue, face, neck and the upper half of the thorax, developing shortly after injection of nicotinic acid and lasting from a few minutes to several hours. All the patients without exception had a normal appetite after from three to four days of treatment. The tongue became normal after from five to six days or earlier. There was cessation of vomiting and gaining of weight in every case. The authors had never observed such a striking gain in weight in pellagra under any other therapy. The effect of the nicotinic acid therapy on the subclinical cases was likewise manifested by a rapid return of the appetite, arrest of diarrhea, improvement in the general condition and a normal appearance of the tongue. The authors conclude that nicotinic acid possesses a powerful specific curative effect on both the well marked and the so-called subclinical cases of pellagra.

Acta Medica Scandinavica, Stockholm

104:527-607 (Aug. 27) 1940

- Parallel Investigations into Ascorbic Acid (Vitamin C) Content in Blood Plasma and into Strength of Cutaneous Capillaries in Healthy Children. N.-G. Ahlberg and G. Brante.—p. 527.
Megalocytic Anemia in Case of Jejunal Ulcer with Fatal Perforation. F. F. P. Weber and H. Huber.—p. 543.
Experimental Chronic Hepatitis (Cirrhosis) Based on Infection. T. T. Andersen and S. Tulinius.—p. 550.
Treatment of Rheumatism with Artificially Ionized Air. A. L. Tchijsky.—p. 561.
Acute Leukemia and "Achronic" Anemia in a Brother and Sister. J. Bichel.—p. 578.
*Hyperthyroidism After Weight-Reducing Thyroidin Treatment. W. T. Andersen.—p. 589.

Hyperthyroidism After Use of Thyroidin for Reducing.—Andersen reports three cases of hyperthyroidism following the use of thyroidin for reducing which were observed at a Copenhagen hospital in the course of one year. The three patients were women past the menopause and all had received energetic treatment with thyroidin. They were hospitalized with severe signs of thyrotoxicosis and auricular fibrillation. The treatment proved more difficult than usual; only two could be brought into a condition suitable for operative treatment. In the third case, however, spontaneous improvement appeared about a year after the onset. Of the cases in which surgical treatment was employed, only one showed a fairly satisfactory response. The hypothesis is advanced that the protracted administration of thyroid might produce a dysfunction of the hypophysis with increased production of the thyrotropic hormone, so that these cases represent a hypophysial rather than a thyrogenic hyperthyroidism. This view seems to be supported by the fact that the enlargement of the thyroid was slight in all three cases and that they were strikingly refractory to the usual treatment. The uncommonly malignant character of the reported cases convinced the author that extreme caution is necessary in the use of thyroid preparations for reducing.

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HYPERTENSION AND THE SURGICAL KIDNEY

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In 1934 Goldblatt,¹ working in the physiologic laboratories at Western Reserve University, reported that partial constriction of the renal arteries of dogs was followed by a rise in blood pressure. Other observers previously had shown that hypertension was related to renal pathologic change, but no one ever had demonstrated it so graphically. Similar experiments were made subsequently in numerous laboratories, most of which confirmed the observations of Goldblatt.

Seldom have physiologic experiments attracted such immediate, widespread interest in medical circles. The etiology and the treatment of hypertension have presented problems which have baffled medical science for long and it is not surprising that any suggestion as to the cause and amelioration of this disease would create general interest. It was not long before Goldblatt's experimental observations were confirmed by clinical reports² of cases in which the blood pressure of patients with hypertension returned to normal after removal of a diseased kidney. These reports of cases seemed to prove that unilateral renal lesions may cause hypertension and that removal of the affected kidney often is followed by recovery.

It seemed to us that a review of a large series of cases in which there were renal lesions which had been subjected to surgical treatment would afford information concerning such problems as the following: (1) the incidence of hypertension in relation to the different types of renal lesions, (2) the postoperative course of the blood pressure in these cases and (3) the relation of hypertension to (a) renal stasis, (b) renal function and (c) bilateral renal involvement.

INCIDENCE OF HYPERTENSION AMONG PATIENTS WITH SURGICAL CONDITIONS OF THE KIDNEY

Before determining the incidence of hypertension in association with renal lesions it seemed desirable to

determine its occurrence in a random group of adult patients. A study was made of the blood pressure readings in 975 consecutive cases taken at random from the registrations at the Mayo Clinic (table 1). Adopting 145 mm. of mercury as the lowest level of abnormally elevated systolic blood pressure, we found that 195 of the 975 patients examined, or 20 per cent of the total, had hypertension. In deference to the opinions of some clinicians, we also kept records which would allow 160 mm. to be considered the lowest level of abnormally elevated systolic pressure (table 2). One is impressed with the influence of age in determining the incidence of hypertension, a factor which is not directly related to a renal lesion. Of the patients who were less than 50 years of age 9.1 per cent had hypertension, while of those who were 50 years of age or more 37.9 per cent had hypertension. Thus the incidence of hypertension in the older group was more than four times as great as it was in the younger group.

In order to determine whether the incidence of hypertension was increased by renal pathologic change observed in the so-called surgical kidney, a study was made of a group of 1,684 patients subjected to renal surgical procedures at the Mayo Clinic (table 2). In this group approximately the same percentage had hypertension as that observed in an average group of adult patients. It could be inferred that many renal lesions of a surgical type do not cause hypertension, since the incidence of hypertension in the group of patients subjected to surgical measures was not higher than that in the average group just mentioned. However, the influence of age on the incidence of hypertension again was found to be a factor, since the incidence of hypertension among patients with surgical kidneys was lowered by the slightly larger percentage of these patients who were less than 50 years of age.

A study of the 315 cases in which surgical lesions of the kidney were associated with hypertension showed that the incidence of hypertension varied widely among the various types of renal lesions concerned. Hypertension occurred most frequently in association with chronic renal infection which caused extensive atrophy of the renal tissues and sclerosis of the blood vessels. Renal infection was not an etiologic factor in hypertension unless it caused widespread atrophic changes in the renal parenchyma. Hypertension occurred much more frequently among patients with atrophic pyelonephritis than among those with any other renal lesion. Such sclerosis may occur either as the result of primary renal infection or secondary to some other renal lesion. The incidence of hypertension in association with surgical pyelonephritis, without atrophic changes, was less than half of that observed in association with diffuse atrophic changes. That some secreting renal tissue remain is necessary, since complete atrophy does not cause hypertension. It is of interest that hypertension afflicted only a small number of patients with acute

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2. Barker, N. W., and Walters, Waltman: Hypertension Associated with Unilateral Chronic Atrophic Pyelonephritis: Treatment by Nephrectomy, *Proc. Staff Meet., Mayo Clin.* 13: 118-121 (Feb. 23) 1938. Butler, A. M.: Chronic Pyelonephritis and Arterial Hypertension, *J. Clin. Investigation* 16: 889-897 (Nov.) 1937. Goldblatt, Lynch, Hanzal and Summererville.¹

renal infection who were subjected to surgical operation; yet this lesion often involved both kidneys. The preoperative blood pressure was normal in all but one of the cases in which operation was performed for perinephric abscess.

In what follows, the number of cases representing the various lesions will not add to the total of 315, because not all types of lesions encountered will be discussed.

Atrophic Pyelonephritis.—In this group were few, if any, clinical data which would enable one to distinguish between the patients who had hypertension and those who did not have it. Although extensive renal and vascular sclerosis was found in most of the kidneys removed in the cases in which hypertension was present, nevertheless similar renal pathologic change was found occasionally in the cases in which blood pressure was normal. It would seem that certain systemic factors exist in one individual which cause hypertension in the presence of a renal lesion but that existence of the same factors does not affect the blood pressure of another individual. It is of interest that, of ten patients with hypertensive atrophic pyelonephritis, seven were females. In contrast to the high incidence of hypertension in association with atrophic pyelonephritis, the blood pressure was normal in five cases in which operation was performed for congenital hypoplasia.

Knowledge of the postoperative course of the blood pressure was available through follow-up records in eighteen of the forty-three cases of atrophic pyelonephritis. In this group of eighteen patients were ten who had had hypertension preoperatively and it was found that the blood pressure of seven of these had returned to normal after operation, while it was not influenced in three cases. Of the eight cases in which the blood pressure had been normal preoperatively hypertension developed after operation in one, while it remained normal in the others. It was difficult to determine, on preoperative clinical examination, whether

Renal Stone.—A review of the blood pressure in 793 cases in which operation was performed for renal stone (hydronephrosis with stone, stone with infection and stone without infection) revealed that there were 161 cases, or 20.3 per cent, in which the blood pressure was 145 mm. or more. Although the statistical incidence

TABLE 2.—Relative Incidence of Hypertension in Association with Renal Lesions: 1,684 Surgical Cases

	All Cases	Hypertension			
		Systolic Blood Pressure, 145 Mm. or More		Systolic Blood Pressure, 160 Mm. or More	
		Num-ber	Per Cent	Num-ber	Per Cent
Adenocarcinoma.....	137	38	27.7	19	13.9
	158	12	7.6	4	2.5
Pyelonephritis other than atrophic.....	43	20	46.5	15	34.9
Hydronephrosis.....	70	13	18.6	6	8.6
Hydronephrosis and stone.....	372	51	13.7	21	5.6
Stone with infection.....	577	121	20.9	82	14.2
Stone without infection.....	164	37	22.5	19	11.6
Miscellaneous.....	62	3	5.7	0	0
	111	20	18.0	9	8.1
Total.....	1,684	315	18.7	175	10.4

of hypertension in association with renal stone did not differ much from the percentage in all cases, the actual incidence of hypertension in association with stone is slightly higher than this survey indicated, because among the patients with stone was a somewhat larger percentage less than 50 years of age. The influence of secondary infection on the blood pressure in cases of stone is shown by the fact that hypertension occurred in 22.5 per cent of cases in which there was manifest infection and in only 5.7 per cent of cases in which there was little or no infection. The degree of pyuria was not the important factor; neither was the reduction in function or urographic deformity of the affected kidney; the extent of atrophic changes in the renal parenchyma and the vascular sclerosis apparently caused the hypertension. It should be noted that in eight, or 40.0 per cent, of the twenty cases of atrophic pyelonephritis associated with hypertension renal lithiasis existed previous to the other conditions. It may be inferred, therefore, that renal stone with atrophic types of infection is a factor in causing renal hypertension. The incidence of hypertension in cases of bilateral stone was found to be no greater than in cases of unilateral stone.

The postoperative course was traced in 189 cases of renal stone. Of this number, in 111 cases hypertension had been present preoperatively and in seventy-eight cases preoperative blood pressure had been normal. The group of 111 cases in which hypertension had been present preoperatively was divided into (1) twenty-five cases in which the blood pressure returned to normal following operation, (2) ten cases in which the blood pressure returned to normal for a variable period after operation but subsequently became elevated and (3) seventy-six cases in which the blood pressure was not altered by surgical measures. It is of interest that the blood pressure returned to normal and remained normal following surgical intervention in approximately 23 per cent of the cases in which hypertension had been present preoperatively. Although nephrectomy was carried out in most of these cases, the blood pressure became normal in many cases following nephrolithotomy. It may be assumed that removal of an irritating and blocking stone

TABLE 1.—Incidence of Hypertension According to Age: Patients Taken at Random, Mayo Clinic, 1938

Age of Patients, Years	Cases	Systolic Blood Pressure, 145 Mm. or More		Systolic Blood Pressure, 160 Mm. or More	
		Cases	Per Cent	Cases	Per Cent
Less than 20.....	57	0	0	0	0
20 to 29.....	146	3	2.1	1	0.7
30 to 39.....	178	15	8.4	9	5.1
40 to 49.....	225	37	16.4	23	10.2
Total less than 50.....	606	55	9.1	33	5.4
50 to 59.....	202	58	28.7	44	21.8
60 to 69.....	118	56	47.4	41	34.7
70 or more.....	49	26	53.1	16	32.7
Total more than 50.....	369	140	37.9	101	27.4
Total for entire group.....	975	195	20.0	134	13.7

nephrectomy would cause reduction in blood pressure. A comparatively recent onset of hypertension, and a short duration of symptoms, with no hypertensive changes in other tissues, seemed to warrant the best prognosis. The percentage of cases in which blood pressure was permanently reduced after nephrectomy for atrophic pyelonephritis (70) was far greater than when nephrectomy was performed for any other type of lesion.

and drainage of infected portions could remove factors which influenced hypertension. In the ten cases mentioned previously the blood pressure returned to normal after operation and remained normal over a period of from six months to two years, but subsequently hypertension returned. Apparently etiologic factors of hypertension may be temporarily allayed by operation, but other underlying systemic factors may reassert themselves subsequently.

It is evident that etiologic factors other than those relative to the kidney were present in the group of seventy-six cases in which hypertension was not affected by operation. In the majority of these cases the renal lesion was unilateral and the failure in reduction of blood pressure could not be explained by any lesion in the other kidney, at least as far as could be determined on careful examination. Although many cases in which nephrectomy was performed were included in this group, in most of the cases a conservative operation had been performed.

Hypertension developed subsequent to operation in twelve cases in which the preoperative blood pressure had been normal. In ten of these cases the increase in blood pressure followed a conservative renal operation. In this group were several cases in which the blood pressure returned to normal following secondary nephrectomy. It can be assumed, therefore, that when hypertension develops following nephrolithotomy the possible development of postoperative nephrosclerosis must be considered and subsequent nephrectomy may be advisable.

Hydronephrosis.—The low incidence of hypertension accompanying hydronephrosis without stone (table 2) can be explained partially by the large number of patients in this group who were less than 50 years of age. Hypertension afflicted only 7.7 per cent of the patients less than 50 years of age and 38.9 per cent of the patients more than 50 years of age. The size of the hydronephrotic sac and the degree of stasis were not a factor, since there was no difference in the incidence of hypertension in the presence of hydronephrosis graded 1 or 2 taken together and in the presence of that graded 4 or more. Bilateral hydronephrosis, which occurs often, was not accompanied by hypertension except in two cases in which bilateral hydronephrosis and acute renal stasis were present. The presence of infection was not in itself an important factor in the presence of hydronephrosis, since the incidence of hypertension in cases in which infection was present was only 14.3 per cent. As was true in the cases of stone and pyelonephritis, the resulting sclerotic and atrophic changes in the renal parenchyma were the deciding factors.

The postoperative course of seventy-three patients operated on for hydronephrosis without stone was traced. Of this number, twenty-nine had had hypertension preoperatively. In forty-two cases the preoperative blood pressure had been normal and remained so and in two other cases, although the preoperative blood pressure had been normal, hypertension developed after operation. Among the twenty-nine cases in which hypertension had been present preoperatively there were ten, or 34.4 per cent, in which the blood pressure returned to normal following surgical measures and remained normal for from one to five years. Nephrectomy was performed in eight of these ten cases and conservative operation in two. The hypertension

persisted in sixteen of the twenty-nine cases in spite of nephrectomy and apparently was not related to renal pathologic change. Although hydronephrosis was bilateral in four of these cases, this did not seem to be etiologic of hypertension, since surgical drainage did not affect it and the function of the two kidneys, taken together, was normal.

Renal Tuberculosis.—In a group of 158 patients operated on for renal tuberculosis hypertension was found in only twelve cases, or 7.6 per cent. Although one might expect a high incidence of hypertension with diffuse tuberculous infection of the kidney, which is often of a cicatricial nature, the contrary was true (table 2). Nephrosclerosis may be present but vascular sclerosis is apparently uncommon in the presence of the renal pathologic changes which occur with tuberculosis. In explaining the low incidence of hypertension the factor of age is of importance, since 132 patients, or 83.5 per cent, were less than 50 years of age.

Hypertension might be expected to occur as a result of the extensive atrophic changes which take place in the tuberculous kidney which has undergone so-called autonephrectomy. However, of a group of thirty-seven cases in which autonephrectomy was diagnosed, hypertension occurred in only five, or 13.5 per cent. There was no increase in the incidence of hypertension among the patients with bilateral renal involvement.

The course of hypertension following nephrectomy for renal tuberculosis is of interest. Eleven patients were traced who had had preoperative hypertension with renal tuberculosis. Of this number the blood pressure of seven returned to normal. The blood pressure of two others remained normal for less than a year and subsequently became elevated. In the two remaining cases the hypertension was not influenced by nephrectomy. It is evident that, although the incidence of hypertension with renal tuberculosis is low, the chance for recovery following nephrectomy is encouraging.

Renal Tumor.—It is evident that the factor of age explains the comparatively high incidence of hypertension in this group (table 2) since eighty-seven, or 63.5 per cent, of these patients were 50 years of age or more. It should also be stated that the blood pressure in most cases was elevated only moderately, since it was below 160 mm. in nineteen, or 50 per cent, of the thirty-eight cases. The possibility of a pressor substance being secreted or of secretion of such a substance being stimulated by the tumor cells has been suggested by several observers and must be considered. Against this hypothesis, however, is the negative evidence obtained by Bradley and Pincoffs³ by means of perfusates in several cases of Wilms's tumor. The large number of patients with hypernephroma whose blood pressure is not elevated would tend to negate the hypothesis of pressor secretion. Secondary renal infection may have some effect on blood pressure, although hypertension was present in only four of twelve cases in which infection was a factor.

There are not enough cases of renal neoplasm other than hypernephroma to allow an accurate survey of each type to be made. Hypertension was noted in six cases of epithelioma of the renal pelvis and the blood pressure returned to normal after nephrectomy in only

3. Bradley, J. E., and Pincoffs, M. C.: Association of Adenomyosarcoma of Kidney (Wilms Tumor) with Arterial Hypertension, *Ann. Int. Med.* 11: 1613-1628 (March) 1938.

one case. The blood pressure was recorded in eighteen cases of Wilms's tumor and definite hypertension was noted in only five.

The postoperative course of forty-three patients operated on for hypernephroma was traced. Preoperative hypertension had been present in twenty-one of these cases. The blood pressure returned to normal after nephrectomy in nine of them; in three of the cases there was a temporary drop in blood pressure, with subsequent hypertension. The hypertension was not affected by nephrectomy in nine of the cases and it could be assumed that extrarenal factors caused the hypertension in this group and that the presence of the tumor was merely coincidental.

Of particular interest was a case of polycystic disease with hypertension in which one kidney had become functionless as a result of diffuse infection. The blood pressure returned to normal following nephrectomy and had remained normal for more than a year when the most recent information was obtained. In another case of polycystic disease, wherein a similar condition was present, blood pressure was temporarily reduced but in a few months hypertension returned.

POSTOPERATIVE HYPERTENSION

The blood pressure of fourteen patients was normal prior to a conservative renal operation, and hypertension developed after the operation. Urologic examination revealed evidence of reduced function and persistent infection in the kidney subjected to previous operation and, after removal of the kidney, the blood pressure became normal. Examination of the removed kidney usually disclosed widespread tissue atrophy and vascular sclerosis, which apparently had resulted from operative trauma and infection. The operations that were performed, or the conditions for which operations were performed, were, as far as we could learn, nephrolithiasis, hydronephrosis, nephrostomy, ureterolithotomy, nephropexy, ureterovaginal fistula following hysterectomy and persistent vaginal fistula. Nephrosclerosis as a cause of hypertension was observed in two cases following severe renal injury. In every case of hypertension in which there was a history of previous renal operation or renal injury, therefore, the possibility of postoperative nephrosclerosis must be considered.

A postoperative increase in blood pressure apparently occurs more frequently following conservative operation for renal and ureteral lithiasis than other lesions. In considering the advisability of nephrectomy in the presence of renal stone and extensive infection, the possibility of subsequent development of sclerotic pyelonephritis with hypertension must be borne in mind. Postoperative renal atrophy and sclerosis may also explain the hypertension which sometimes is observed following transplantation of the ureters into the sigmoid. Postoperative urographic examination in two of these cases revealed that one kidney was functionless and exploration of the affected kidney disclosed widespread sclerotic changes as the result of infection and stasis. Removal of the affected kidney was followed by restoration of the blood pressure to normal.

RENAL INSUFFICIENCY

Renal insufficiency was not found to be etiologic of hypertension in the cases in which renal surgical operation was performed. In cases in which bilateral stone and hydronephrosis were present, together with moderate impairment of function of both kidneys, and in which both kidneys were subjected to conservative operation,

the incidence of hypertension was not greater than in similar cases in which function was not impaired. Among patients with insufficiency of both kidneys, who were examined but not operated on because of low renal function, the incidence of hypertension was only a trifle higher than in the random group.

RENAL BACK PRESSURE

Renal back pressure is not of much significance in causing hypertension. The average blood pressure in cases in which the hydronephrotic sac was large or in cases of bilateral hydronephrosis was no higher than normal. Hypertension developed in two cases of bilateral hydronephrosis in which one kidney suddenly became occluded and it was relieved in one of these cases by renal drainage.

CONTRAINDICATIONS TO SURGICAL INTERVENTION

Hypertension is caused by factors other than those relative to the kidney in most cases and the presence of a surgical kidney may be of only coincidental clinical significance. This is proved by the large number of cases in which hypertension is present but there is no reduction in blood pressure following removal of a diseased kidney. Nephrectomy may be contraindicated in cases in which hypertension accompanies a surgical renal lesion if any of the following factors are present: (1) bilateral renal disease so extensive that removal of one kidney would be of no benefit; (2) the existence of hypertension of long standing, with such extensive secondary degenerative lesions in other organs that removal of a diseased kidney would no longer influence the subsequent clinical course; (3) evidence of advanced renal insufficiency, and (4) existence, in another organ, of an unrelated serious lesion which in itself might be regarded as inoperable.

COURSE OF BLOOD PRESSURE AFTER OPERATION

The postoperative course of the blood pressure was followed in 372 cases in which surgical operation was performed on the kidney. All these patients were traced for at least six months, the majority of them for more than a year and, in several instances, for as long as five years. Preoperative hypertension had been observed in 198 of these cases and the preoperative blood pressure had been normal in 174 cases. Hypertension was permanently relieved by surgical operation for various renal lesions in sixty-five, or approximately a third, of the 198 cases. Hypertension in the presence of surgical lesions of the kidney was relieved more often by nephrectomy than by conservative operation.

In seventeen cases there was a postoperative drop in blood pressure but the hypertension returned within a few weeks or months following operation. A temporary drop in blood pressure, occurring immediately after operation, often is caused by rest in bed and removal of a toxic irritant. In several cases the blood pressure remained normal as long as two years after operation and then returned to the preoperative level. In such cases it may be inferred that primary hypertension existed and had been temporarily increased by a surgical renal lesion. In order to determine the permanent result of the operation it is necessary to follow the patient's blood pressure for at least two years. There were 117 cases in which alteration in blood pressure did not take place as a result of surgical operation on the kidney. Since evidence of disease of the other kidney could not be determined by careful examination, it would be logical to assume that all these

patients were suffering from so-called essential hypertension and that their condition was not influenced by a renal pathologic condition, at least of a surgical nature. Included in this group were seventy-two cases in which nephrectomy was performed and forty-five in which the operation was conservative. Among the cases in which preoperative blood pressure was normal, hypertension developed subsequent to operation in twenty. Several cases were included in this group in which the increased blood pressure was caused by postoperative nephrosclerosis and in which subsequent nephrectomy caused the blood pressure to return to normal.

COMMENT AND SUMMARY

Hypertension occurring in the presence of a unilateral lesion of the kidney was frequently relieved by surgical operation on the kidney.

The incidence of hypertension in a group of 1,684 patients subjected to renal surgical operation was no higher than it was in a group of patients taken at random. In a study of the incidence of hypertension the factor of age is of importance.

The renal lesion amenable to surgical treatment which occurs most often in association with hypertension is atrophic pyelonephritis. This lesion is the result of extensive infection and is characterized by widespread atrophy of the renal tissues and sclerosis of the renal blood vessels; apparently this process causes hypertension. Hypertension afflicted twenty of forty-three patients operated on for primary atrophic pyelonephritis, or 46.5 per cent. The incidence of hypertension is low in cases in which operation is performed for pyelonephritis without atrophy and sclerosis. Acute cortical renal infection or perinephric abscess is seldom a factor in causing hypertension.

Hypertension was observed in 161 cases, or 20.3 per cent, of 793 cases in which operation was performed for renal stone. The role of secondary infection is important, since hypertension occurred in 22.5 per cent of cases in which infection was manifest and in only 5.7 per cent of cases in which there was no infection. However, the deciding factor was not the degree of infection but the presence of extensive vascular sclerosis and parenchymal atrophy.

Hypertension was noted in approximately 14 per cent of cases of hydronephrosis without stone for which operation was performed. As with renal stone, the presence of tissue atrophy and vascular sclerosis seemed to affect the blood pressure. The degree of pyelectasis did not seem to be a factor, since the incidence of hypertension was no greater in cases in which pyelectasis was of grade 4 than in cases in which it was of grade 1.

Hypertension was observed less frequently in the presence of renal tuberculosis than as an accompaniment of most other forms of surgical kidney. It was present in twelve, or 7.6 per cent, of the 158 cases of renal tuberculosis studied.

Hypertension was found in thirty-eight cases, or 27.7 per cent, of 137 cases in which operation was performed for renal adenocarcinoma. The comparatively high incidence of hypertension in this group of cases is increased by the factor of age, since eighty-seven patients, or 63.5 per cent, were in the sixth decade of life or older. The exact influence of the neoplasm is obscure; the secretion of a pressor substance has been surmised, but corroboratory chemical and physiologic evidence is wanting.

Hypertension may develop in a variable time after a previous conservative renal operation. In many of these cases the blood pressure becomes normal after removal of the affected kidney. In every case of hypertension in which there is a history of previous operation, the possibility of postoperative nephrosclerosis must be considered.

Renal insufficiency apparently is not a factor in causing hypertension. In most cases of hypertension no evidence of reduced renal function was found. On the other hand, many patients whose renal function was reduced had no hypertension.

Back pressure as the result of renal stasis usually is not a factor in hypertension unless acute bilateral obstruction is present.

The discovery of a unilateral renal lesion in the presence of hypertension does not indicate that operation is advisable in every case, since other factors are often present which would contraindicate it.

Bilateral renal involvement, such as occurred in many cases of renal stone, hydronephrosis and renal tuberculosis, was not an etiologic factor in hypertension.

A follow-up study was made in 198 cases in which hypertension was present and in which surgical operation was performed. The blood pressure became normal after operation in sixty-five, or a third, of the cases and remained normal for a year or more.

It may be predicated that hypertension will be relieved by surgical operation in approximately 70 per cent of cases in which it accompanies atrophic pyelonephritis, in 50 per cent of cases in which it is associated with renal tuberculosis and in 25 per cent of cases in which it is an accompaniment of renal stone, hydronephrosis or tumor.

Although hypertension which is associated with surgical lesions of the kidney is relieved more often by nephrectomy than by conservative operation, the blood pressure often returned to normal after nephrolithotomy and renal drainage.

Reduction in blood pressure may exist as long as a year or more after operation and yet hypertension may return. This may be explained on the ground that a toxic or irritant lesion has been eliminated and, when this influence has worn off, the underlying essential hypertension reasserts itself. In order to determine whether recovery after operation is permanent it is necessary to determine the patient's blood pressure for more than a year.

Hookworm.—Hookworm disease in the United States is due to *Necator americanus* (except in a small area in California). The adult parasite lives in the upper part of the small intestine, where it is attached to the mucosa and sucks blood from the host, so that the essential clinical picture is one of anemia. The degree of clinical symptomatology depends in general on the number of parasites harbored. Ova are discharged in the feces and hatch only on exposure to the air. The larvae live in the soil and pass through several molts until the infective stage is reached. Invasion of the host occurs in practically every instance through the bare skin, usually of the foot. The larvae penetrate to the lymph circulation, thence through the general circulation to the lungs. They pass through the alveoli to the bronchial tree and are carried up to the posterior nasopharynx and swallowed. Once in the small intestine, the adults fasten themselves to the mucosa and are removed with difficulty. They may live for five years or longer.—Smillie, Wilson G.: Public Health Administration in the United States, New York, Macmillan Company, 1940.

VASCULAR NEPHRITIS AND HYPERTENSION

A COMBINED CLINICAL AND CLINICOPATHOLOGIC
STUDY OF 150 NEPHRECTOMIZED PATIENTS

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In recent years, medical interest has been centered on the problem of hypertension. Although it was in 1827 that Bright connected the condition of the kidney with blood pressure and there have been frequent observations of the relation of cardiac hypertrophy to surgical renal disease which date back as far as 1835, it remained for Goldblatt's¹ work on experimentally produced hypertension in dogs and monkeys to reawaken interest in the subject and open a new and profitable approach to experimentation.

Renal ischemia may be produced in a variety of ways. In addition to the classic experiments of Goldblatt and the recording of numerous instances of hypertension in polycystic kidneys and hydronephrosis, one must con-

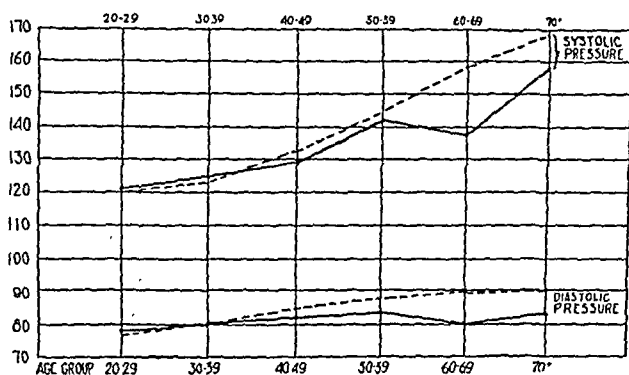


Fig. 1.—Comparison of blood pressure of age groups with "normal." Solid line, 150 nephrectomy cases; broken line, 5,540 cases compiled by Wetherby (average of males and females, Berglund and Medes¹⁰).

sider arteriosclerotic plaques of the renal artery and pyelonephritis as causal factors.

Blackman² examined fifty cases of "essential" hypertension and fifty control cases without hypertension and found arteriosclerotic plaques causing reduction in the lumens of one of each of the main renal arteries in forty-three (86 per cent) of the cases with hypertension. The control cases showed only five (10 per cent) with comparable lesions. It should be accepted that renal ischemia can cause hypertension under certain conditions.

Longcope³ studied the relation of bilateral chronic pyelonephritis to hypertension in cases ending fatally. He concluded that the factor involved in the production of hypertension was not associated with renal failure.

Weiss and Parker⁴ concluded that pyelonephritis is often associated with arterial hypertension and that vas-

cular changes frequently occur. They further concluded that there is a great tendency toward severe hypertension in patients with pyelonephritis and that pyelonephritis is responsible for at least 15 to 20 per cent of cases of malignant hypertension. They seem to imply that the sequence of events in pyelonephritis leads to the terminal stage of severe hypertension. With certain reservations in mind, it should be accepted that pyelonephritis causes renal damage which may in turn lead to hypertension. The exact nature of the specific lesion causing hypertension is doubtful at least.

Butler⁵ in 1937, and later Leadbetter and Burkland,⁶ reported cases of unilateral renal disease associated with hypertension in which apparent cure of the hypertension was produced by nephrectomy. Many other observers⁷ soon followed with well studied case reports, and many more will undoubtedly soon be added. These cases have been carefully studied and may be accepted as proved, representing another phase of the problem of hypertension. We must therefore accept the evidence that unilateral renal disease is capable of producing hypertension and that the blood pressure is influenced favorably by elimination of the diseased kidney in some cases.

In spite of these authentic instances, which even now do not comprise a large group of cases, it has appeared to urologists that this association of renal disease with hypertensive cases is not the rule in urologic practice. The challenge to the urologist's concept has been accepted by Crabtree and Prien⁸ and by Mulholland.⁹

It is our purpose in this study to examine, through the specimen obtained by nephrectomy, with respect both to hypertension and to vascular changes in the kidney, a series of routine urologic cases which often represent long standing, severe degrees of unilateral renal damage. Such a study affords a mean of examination of the pathologic processes in the kidney, together with clinical end results of therapy.

One hundred and fifty almost consecutive nephrectomized patients were studied urologically and by pathologic examinations of the removed kidneys. The pathologic studies were detailed, in that examinations of the more normal portions of the kidneys were made as well as of the grosser aspects of the lesion present. Special attention was given to the condition of the blood vessels in both the more normal and the more diseased portions of the specimens.

The age, sex and blood pressure of these cases is shown graphically in table 1. These statistics are quite comparable to those compiled by Wetherby¹⁰ in a statistical study of 5,540 normal individuals. The blood pressure determination of any individual was arrived at by study of all known blood pressure readings before

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operation. Immediately preoperative readings were not used because of the effect marked sedation has on the lowering of blood pressure. Cases in which there were long intervals between known pressures were deter-

The effect of emotion on blood pressure has been shown conclusively by Alexander¹¹ to cause definite elevation. The averages shown by him were 19 mm. of mercury systolic and 12 mm. diastolic pressure. In our figures we have not made allowance for these cases. The blood pressure readings are taken as they have been



Fig. 2.—Section of the cortical portion of a chronic pyelonephritic kidney from a patient without hypertension. The glomeruli show various stages of hyalinization and interstitial infiltration.

mined by taking the average of the recent readings, excluding the remote pressures. Some of our patients had only one preoperative blood pressure determination, which was usually taken the night before operation.



Fig. 3.—Section of the tubular portion of the same kidney as in figure 2. Note a sclerosed vessel in the right upper portion and hyaline debris in lumens of tubules.

These readings will tend to give our averages a higher value, since excitement and nervousness definitely elevate blood pressure. This has been found to be a factor in many cases which have been followed carefully since the present study was begun.

TABLE 1.—Age, Sex and Blood Pressure

Age Group	Total Number in Group	Number of Males	Number of Females	Average Age	Average Systolic Blood Pressure	Average Diastolic Blood Pressure
10-19	1	0	1	12	138	85
20-29	21	9	12	25.8	122	78.4
30-39	35	9	26	34.4	125.7	80.1
40-49	34	17	17	44.3	128	80.9
50-59	43	21	22	52	142.4	82.8
60-69	12	7	5	62.4	137.5	79.4
70+	4	2	2	73	156	80
Averages Totals	150	65	85	132.3	81.2

recorded. Despite this, a comparison with the average blood pressures of men and women in Wetherby's study shows the averages of our severe renal damage group

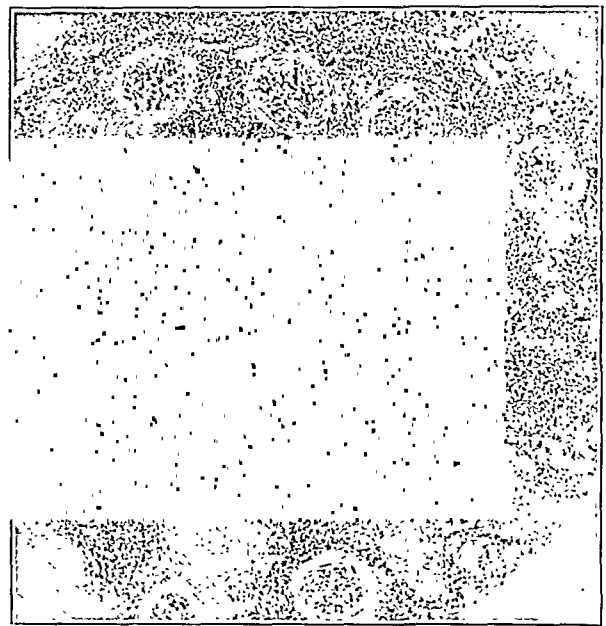


Fig. 4.—Section from the cortical portion of the kidney from a case of chronic pyelonephritis without hypertension. The tufts of the glomeruli are in fairly normal condition but thickening of the peripheral layer of Bowman's capsule characterizes this lesion.

to be somewhat lower. This comparison has been charted in figure 1. A comparison of age group 10-19 has been omitted, since only one case fell into this group. The figures for charting Wetherby's averages were obtained by averaging his readings for men and for women in the same age group. This was necessary, since the groups studied and recorded related to both sexes.

It might be argued that hypertensive cases might be hidden by averaging large groups of individuals. In order to study more in detail the actual presence of hypertension in this series, all cases showing blood pressures above 150 systolic, 100 diastolic, were further investigated. Fourteen cases were found. The age groups, the blood pressure, and the pathologic condition are shown in table 2. Follow-up blood pressure readings were obtained of twelve of these patients and have

11. Alexander, Franz: Psychoanalytic Study of a Case of Essential Hypertension, *Psychosom. Med.* 1: 139 (Jan.) 1939.

been recorded. No follow-up was obtained of the other two patients because they could not be located.

The pathologic conditions found in this survey are shown in table 3. The types of disease and age distribution of this group are strikingly similar to the summary of 180 cases of nephrectomy recently reviewed by

TABLE 2.—Cases (Fourteen) with Hypertension and Follow-Up Blood Pressure

Age Group	Total Number in Group	Cases with Hypertension	Pathologic Condition	Degree of Renal Vessel Damage	Post-operative Blood Pressure	Months Post-operative
30-39	35	154/105	Tuberculous pyelonephritis	0	144/80	14
40-49	34	166/100	Chronic pyelonephritis	++	160/90	29
		165/95	Chronic pyelonephritis	0	160/110	43
50-59	43	178/105	Hypernephroma	+++	160/100	2
		238/128	Hypernephroma	++	214/140	18
		160/100	Hypernephroma	++	180/88	4
		180/100	Chronic pyelonephritis	+	*	*
		160/100	Hypernephroma	+	139/68	60
		160/100	Chronic pyelonephritis	++	190/110	7
60-69	12	165/85	Chronic pyelonephritis	0	140/70	39
		160/78	Chronic pyelonephritis	+++	190/80	44
		170/110	Chronic pyelonephritis	++	169/80	57
70+	4	176/98	Hypernephroma	++	*	*
		192/82	Hypernephroma	0	172/100	1

* No follow-up study obtainable.

Deming.¹² The age distribution of the neoplastic group is quite consistent with the 642 cases of renal neoplasia studied by Priestley.¹³ The cases here presented may be considered representative of severe unilateral renal damage.

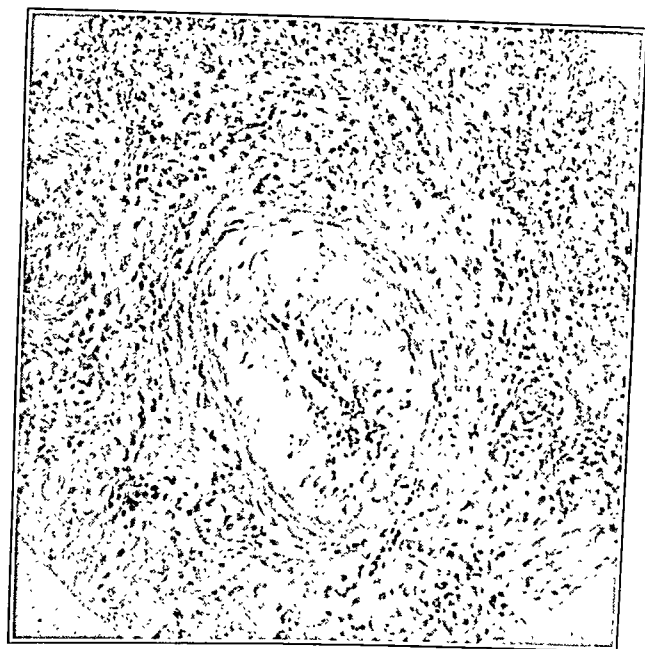


Fig. 5.—Section of pyelonephritic kidney of patient without hypertension. Lesion of grade 3 as defined in text. In figures 5, 6 and 7 note that the lesions occur in the larger arteries of the kidneys and that the sclerosing process involves the circumference of the vessels and that the lumens of the vessels are greatly reduced in size.

The microscopic study of these cases was particularly detailed, with special attention given to inflammatory

and blood vessel changes. Of our 150 cases, ninety-nine (66 per cent) showed chronic renal infection. The degree of damage varied in each case, of course, but all cases showed marked hyalinization and fibrosis of glomeruli in portions or all parts of the specimen.



Fig. 6.—Section of pyelonephritic kidney of patient without hypertension. Lesion of grade 3.

Examples of the glomerular changes are shown in figures 2, 3 and 4. The changes depicted here were common in the majority of this group.

The nature of the influence which marked alteration of glomerular pattern has on the vascular tree is doubtful at the present time. MacCallum¹⁴ has shown that there is an intraglomerular circulatory readjustment of

TABLE 3.—Pathologic Types

Age Group	Hypernephroma or Other Neoplasm	Chronic Pyelonephritis with Hydronephrosis with or without Nephrothiasis	Chronic Pyelonephritis with Contraction	Tuberculous Pyelonephritis	Congenital Abnormalities Including Hypoplasia	Traumatic	Nephrothiasis with Normal Renal Tissue	Actinomycosis	Cystic
10-19	..	1
20-29	..	1
30-39	..	19
40-49	..	20
50-59	..	16
60-69	..	5
70+	..	1
Totals	41	69	7	23	3	1	4	1	1

the vascular pattern, with normally occurring pathologically changed glomeruli in mammals other than man. The exact changes which he described may not apply to man, but it seems safe to assume that some change definitely takes place. Our interest here was not primarily with the pattern of the change but rather with the degree of narrowing of vessel lumens. On a purely arbitrary basis we have classified the vessel changes into three categories, first degree representing small but definite narrowing of the lumen and third degree

12. Deming, C. L.: The Future of the Unilaterally Nephrectomized Patient, *J. Urol.* 40:74 (July) 1938.

13. Priestley, J. T.: Survival Following Removal of Malignant Renal Neoplasms, *J. A. M. A.* 113:902 (Sept. 2) 1939.

14. MacCallum, D. B.: The Bearing of Degenerating Glomeruli on the Problem of the Vascular Supply of the Mammalian Kidney, *Am. J. Anat.* 65:69 (July) 1939.

representing marked narrowing, almost to the point of complete occlusion, with second degree representing the intermediate changes. Examples of third degree occlusion are shown in figures 5, 6 and 7, second degree in figure 8 and first degree in figure 9. We realize fully that we have no yardstick or exact measurements by which an accurate estimate of arterial occlusion can

TABLE 4.—Renal Vessel Changes

Pathologic Condition	Total Cases	Number Percentage of Cases Showing Renal Vessel Changes		Degree of Vessel Damage		
		Vessel Changes	Showing Renal Vessel Changes	1°	2°	3°
Hypernephroma or other neoplasm.....	41	10	24.4	4	4	2
Chronic pyelonephritis with hydronephrosis with or without nephrolithiasis....	69	34	49.3	14	16	4
Chronic pyelonephritis with contraction.....	7	3	42.8	2	1	0
Tuberculous pyelonephritis.....	23	9	39.1	7	2	0
Congenital abnormalities including hypoplasia.....	3	0	0	0	0	0
Traumatic kidney.....	1	0	0	0	0	0
Nephrolithiasis without renal damage.....	4	0	0	0	0	0
Actinomycosis.....	1	1	1	0	0
Cystic.....	1	1	0	0	1
Totals.....	150	58	38.6	28	23	7

Of 150 cases, 99 (66%) showed renal infection.
Of 99 cases, 46 (46.4%) showed renal vessel changes.
Of 58 cases with vessel changes, 46 (79.3%) showed renal infection.

be determined in this present study. We do believe, however, that narrowing to the degree shown in these illustrations may well produce ischemia. All pathologic sections used in illustration are from cases without hypertension.

The changes in renal vessels in our study are shown in table 4. The tabulated results represent, in each case,



Fig. 7.—Section of pyelonephritic kidney of patient without hypertension. Lesion of grade 3.

an evaluation of the stages of the pathologic processes which occur in the kidneys. The degree of narrowing is not determined by the condition of a single isolated vessel. On the whole it was found to be the rule that, if the vessels of the most damaged portions of the kidneys were changed, some degree of change was

present throughout the whole of the kidney. No portion of such kidneys from which sections were taken appeared to have normal vessels. We have classified the kidneys on the vascular condition of the vessels in the major proportion of the kidney. In all, approxi-



Fig. 8.—Grade 2 lesion as described in the text. Note that the vessel wall change is confined to but a portion of the circumference of the vessel.

mately 1,500 pathologic sections were examined. In the entire group, fifty-eight cases showed definite renal vessel changes. In the infectious group, which represented 66 per cent of the total group, we found forty-six (79 per cent) of the vessel changes. The group of chronic pyelonephritis with hydronephrosis showed that approximately 50 per cent had renal vessel changes.

COMMENT

We have attempted to evaluate the hypertensive tendency in 150 cases representing severe unilateral renal damage. Hypertension is not characteristic of these cases. A comparison with average blood pressure readings for the age groups indicates that our cases average slightly lower than normal. The possibility that a hypertensive tendency might be hidden by averaging large groups has been considered. In table 2, all cases showing hypertension have been reviewed. Only fourteen cases showed hypertension. Six of these were hypernephroma, seven chronic pyelonephritis and one tuberculous pyelonephritis. The cases showing the severest hypertension occurred in hypernephroma, in which the age often was in the higher brackets.

The follow-up study on those cases which showed hypertension failed to show any definite trend toward improvement in blood pressure readings after nephrectomy. Two cases showed slight improvement; one hypernephroma and one chronic pyelonephritis. In two cases there was no follow-up.

An attempt to correlate hypertension and renal vessel change also met with failure. Again we recognize that our method of study furnishes no basis for estimating the production of renal ischemia. The total number of cases which showed hypertension is far too few in comparison with the large number which showed renal vessel changes to establish a sufficient correlation to

indicate that renal biopsy is a worthwhile diagnostic measure. Three of our cases of hypertension showed no alteration in renal vessels.

SUMMARY AND CONCLUSIONS

1. One hundred and fifty approximately consecutive nephrectomies were studied. These cases were representative of severe unilateral renal damage.

2. Hypertension was not a common finding in the clinical picture in this group.

3. Vascular changes, which have been considered to be causative factors in the production of hypertension, were present in a high percentage of our cases.

4. Elevation of blood pressure readings was not the rule, even in chronic pyelonephritis, in these cases. Nephrectomy was not followed by appreciable reduction in blood pressure readings before operation.

5. The exact etiologic factor in renal (ischemic) hypertension is as yet unknown. The pathologic and anatomic elements seem less important than an as yet unknown physiologic element.



Fig. 9.—Grade 1 changes in an artery of a pyelonephritic kidney. Note that there is uniform change throughout the circumference of the vessel but that the lumen is not extensively narrowed.

6. Evidence is not produced by this study to encourage employment of nephrectomy in hypertensive cases, except for recognized surgical indications.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. BRAASCH, WALTERS AND HAMMER
AND DRS. CRABTREE AND CHASET

DR. STANFORD W. MULHOLLAND, Philadelphia: A year ago I was interested in experimental work regarding interference with the circulation to the kidney. I was reading isolated reports by surgeons who had found that certain of their patients with single kidney involvement would have diminution in their blood pressure following unilateral nephrectomy. It was necessary to go back and look at the cases in which I had operated previously with extensive kidney damage in order to correlate the experimental work. Dr. Braasch and Dr. Crabtree have reviewed large numbers of cases and have given interesting facts. The work they have done helps to make one realize that the problem is still physiologic. It is still a problem in which one must be looking for the element that is the underlying principle producing the result: the hypertension. Infection, malposition and stone causes blood vessel changes but the result is not always the same. Longcope has summarized our present knowledge of this mystery. He reminds us that no one has been able to tell why one patient develops hyper-

tension long before there is any evidence of renal insufficiency and another patient develops hypertension only after there has been marked renal damage, while at the same time a third patient may die of uremia without having any hypertension. Physiologists have called attention to the fact that a preponderance of the work done by the kidney is accomplished by tubular excretion. It has been found that a comparatively small amount of the work is done by glomerular filtration. Perhaps it is the variation in the degree of damage to the real working renal mechanism that causes the development of this picture we know so well. It is an open challenge to be looking out for these cases that might fall into the group that will be aided by operation. We in Philadelphia are still reviewing our cases with the idea of trying to locate the influencing factor.

DR. ROY J. HOLMES, Miami, Fla.: The observation of Drs. Braasch, Walters and Hammer that atrophic pyelonephritis is the only type of surgical renal lesion associated with hypertension which can be removed with a degree of confidence is in keeping with my own experience. Renal anemia from defective arterial development is a possible factor and may manifest itself only by a reduction in the number of normal renal units and in the rate of renal blood flow. In studying the blood supply in two cases it appears to me that acquired atrophic pyelonephritis may readily be confused with congenital partial hypoplasia or anemia, on which a mild infection may or may not have been superimposed. Abnormalities and extreme variations of the renal artery are very common. In the two families I have known in which almost every member suffered from hypertension at an early age, the percentage of renal deaths seemed to be unusually high. It is pure speculation to suggest that this may throw some light on the well known familial or hereditary tendencies in some cases of hypertension. I am convinced that a kidney not already a legitimate candidate for nephrectomy should be sacrificed only if the kidney under suspicion is markedly reduced in size as compared with its normal fellow. The paper of Drs. Crabtree and Chaset is a much needed contribution tending to clarify the relation between the field of surgical renal pathology and hypertension and possibly directing attention more to renal anemia in which hyalinization, thickening of the arterioles and even functional impairment are secondary, not primary, factors. That degenerative changes are not always the measurement of renal ischemia is illustrated by many of Goldblatt's experiments in which little if any changes could be found in the renal unit or in its functional ability. Since endeavoring to institute methods of estimating the physiologically effective rate of renal blood flow, I feel that this, together with an accurate estimation of the size of the renal excretory mass, may give a faint answer to the challenge which, as Drs. Crabtree and Chaset say, still exists. We are indebted to Drs. Crabtree and Chaset for showing us that hypertension is rarely found in candidates for nephrectomy. We can, however, find considerable reward and encouragement by looking for small unilateral sclerotic kidneys with little if any urinary symptoms in hopeless victims of essential hypertension.

DR. EARL E. EWERT, Boston: Such papers as these will help form a standard in governing one's action toward patients suffering with various types of unilateral disease. Most of us are here in order to crystallize our attitude. In short, we are afraid on the one hand to allow patients with unilateral lesions and hypertension to go on if help can be given and, on the other hand, we wish to avoid unnecessary surgery. I think that if we come down to the crux of the situation, this is our attitude.

DR. JAMES F. McCAHEY, Philadelphia: Skepticism about a connection between the kidneys and hypertension has been engendered by what the authors have called "enthusiastic" reports. Nevertheless, such a relationship is suggested by recent experimental and clinical observations which appear to be sound. The experimental evidence has been furnished chiefly by Goldblatt. Page has described another interesting form of experimental hypertension. He found that, if the kidneys of dogs are surrounded with cellophane or silk, a fibrous hull is formed and hypertension follows. Removal of the hull causes a return of the blood pressure to normal. Performing this

procedure on one kidney only causes a moderate elevation of the blood pressure. It is evident that hypertension in human beings differs in important essentials from the experimental form. It seems established that narrowing of the lumen of one renal artery may cause sustained hypertension with serious sequelae. Nephrectomy may be beneficial. Cases of this kind are unusual and an accurate diagnosis is hardly ever possible prior to operation. Therefore, the pressing problem here is for improvement in method of recognizing cases belonging to this category. It is also evident that the disease which we call "essential hypertension" is not a surgical renal consequence. The finding by Drs. Crabtree and Chaset that vascular occlusive changes may be present in the kidney without hypertension is in accord with the opinion of Fishberg, who believes that the essential pathologic condition is generalized arteriosclerosis. Drs. Braasch, Walters and Hammer find that conservative treatment of various surgical renal lesions will often result in a lowering of the blood pressure in patients with a higher than normal reading. They report certain instances of surgical renal conditions associated with hypertension in which the blood pressure did not fall to normal after nephrectomy and interpret this as indicating that the cause of the hypertension was extrarenal. However, the possibilities that the increased vascular pressure depended on a lesion in the opposite kidney must be kept in mind, since the fact that a kidney responds normally to our present tests does not mean that it does not contain arteriolar changes which lead to some degree of hypertension. The onset of such changes in the remaining kidney may likewise explain the occurrence of hypertension some time after nephrectomy. Both papers are in agreement that nephrectomy for hypertension is indicated only in recognized renal surgical conditions. In the present state of our knowledge, this is sound policy.

DR. GEORGE W. FISH, New York: The excellent papers by Dr. Braasch and Dr. Crabtree and their collaborators form a basis for the surgical treatment of certain cases of hypertension. Both workers have arrived at essentially the same conclusions and their methods of selecting cases are marked by a fine conservatism. During the past three years, Schroeder and I have studied and done nephrectomy in a group of hypertensive patients from 16 to 32 years of age with unilateral renal lesions, at least as far as we were able to establish such a diagnosis by intravenous and retrograde urography, separate phenol red and urea clearance determinations of the kidney, and cultures of separated ureteral specimens. Even with all these tests the presence of bilateral lesions is not always ruled out. Perhaps most important of all, the time of the onset of hypertension in these cases was known, and those whose hypertension did not extend beyond two years responded most favorably. These cases were reported in the May 1940 issue of the *American Journal of the Medical Sciences*. These points and the one made by Drs. Crabtree and Chaset concerning biopsy for diagnostic purposes are brought out by a recent case: A white man aged 40 had a stone removed from the right kidney through a pyelotomy incision in February 1937; the blood pressure was 130 systolic, 90 diastolic. In August 1937 the blood pressure was 148 systolic, 100 diastolic. Two attacks of pyelitis on the right side occurred between that date and April 1939; the blood pressure was 165 systolic, 120 diastolic. I saw the patient first in October 1939; the blood pressure ranged from 212 systolic, 140 diastolic to 154 systolic, 100 diastolic. The symptoms were headaches and lassitude. Three months' observation revealed that both kidneys were functionally normal as determined by the phenolsulfonphthalein and urea clearance tests. The right kidney had some pus and colon bacilli. The left kidney was normal. Increase occurred in hypertension and the size of the heart during the observation period. Right nephrectomy was done Jan. 28, 1939. Marked fall of blood pressure occurred to normal levels. Death occurred on the nineteenth day after operation of pulmonary embolus. This and other reported cases and experimental work suggest that the sclerosis described by Dr. Braasch and his collaborators may not be the cause of the hypertension and that the hypertension may be the cause of the sclerosis. Nephrectomy may prove of benefit but, it seems, only for patients in whom the existence of hypertension is of short duration and in whom

arteriolar sclerosis of the other kidney is not advanced. Its use is probably limited therefore to a small number of hypertensive patients and they remain potentially hypertensive.

DR. WILLIAM F. BRAASCH, Rochester, Minn.: One lantern slide which I did not show contained detailed information concerning the group of fourteen patients who had previously been operated on and who developed postoperative hypertension. Injury to the ureters or kidneys occurred in the course of hysterectomy, various other operations for pelvic disease, vesicovaginal fistulas, nephropexy, ureterolithotomy and nephrolithotomy. In one case, which is of particular interest, both ureters had been transplanted into the rectum and several years afterward hypertension developed. One kidney was infected and atrophic and after its removal the blood pressure returned to normal. It may be inferred, therefore, that when hypertension develops after operations involving the urinary tract the possibility of postoperative nephrosclerosis must be considered. Although the incidence of hypertension caused by unilateral surgical renal lesions is relatively low, nevertheless the more one looks for such cases the more often will one find them. It is a condition which the urologist may not see primarily because the urinary symptoms and signs are often obscure. The patient usually comes first to the internist, who often is not on the lookout for surgical renal lesions unless he is familiar with this possibility. This was well illustrated recently by a patient who came to the Mayo Clinic because of headache. The internist who examined him found hypertension, and although only an occasional pus cell was found in the urine he included roentgenography of the urinary tract among the routine diagnostic procedures. The roentgenogram was reported to be negative. The internist, however, was on the lookout for the possibility of renal disease as the cause of hypertension, so he reviewed the roentgenogram himself and saw that the outline of one kidney was definitely smaller than the other. Then he called in the urologist, who also found the difference in renal outlines and suggested that an excretory urogram be made. The urogram visualized deformity typical of atrophic pyelonephritis in one kidney and showed that the other kidney was normal. Nephrectomy was advised and the blood pressure returned to normal subsequently. This field offers the urologist one of the most promising opportunities for clinical investigation. Judging from the statistics I have shown, there can be no doubt as to the efficacy of renal surgery in reduction of blood pressure in certain carefully selected cases.

DR. NATHAN CHASET, Boston: In our study we have found severe pathologic changes without finding hypertension to any extent. The reason has not been obvious, and we have come to believe that some physiologic or chemical process initiated by the kidney is probably responsible for the production of hypertension in many cases, but that equally potent forces in the body can be marshaled to combat it. The role the kidney plays in the production of hypertension is not clear. The work of Page and his associates is probably nearer the true concept than others presented. It is as follows: Experimentally produced hypertension, either by Goldblatt's method or by the method of Page, is caused by the liberation from the kidney of an enzyme-like substance which is called "renin." Renin alone causes no hypertension. It requires a kinase-like material contained in the protein fraction of plasma and whole blood. It has also been shown that tachyphylaxis to renin develops rather rapidly, owing to exhaustion of renin activator. When tachyphylaxis develops in the presence of excess renin, further addition of renin activator does not restore the pressor effect of renin. It appears that some substance develops which prevents the combination of renin and renin activator. This has been called the antipressor state, or renin inhibitor. The interaction of renin and renin activator yields "angiotonin," a highly active pressor substance. Whereas renin causes tachyphylaxis quickly as the result of depletion of renin activator, angiotonin causes only mild tachyphylaxis after many injections. Angiotonin appears to be an intermediate rather than an end product in the interaction of renin and renin activator. It also requires an activator which differs from renin activator. The mechanisms for the production of tachyphylaxis to renin and angiotonin are interrelated. It seems to be due to the

exhaustion of their respective activators as well as to the development of inhibitors. Thus experimentally it seems that there are potent substances capable of vasoconstriction which are liberated by the kidney under certain conditions. There are also equally potent and effective mechanisms for the prevention of the vasoconstrictor action. Studies on the inhibitor mechanisms are being carried out at the present time.

TREATMENT OF COMPOUND FRACTURES IN WAR

REPORTS OF PRACTICAL EXPERIENCE IN THE
SPANISH CIVIL WAR

LEO ELOESSER, M.D.

SAN FRANCISCO

It was evident to surgeons who took part in the late civil war in Spain that modern warfare was to differ greatly from previous wars and that the difference would be due to advances in the mechanics of transportation and especially to extensive use of aviation. It was apparent that surgeons had much to learn and to unlearn in matters of organization, in evacuation of wounded and also in the treatment of war injuries. Especially noticeable was distrust in chemical antiseptics. Irrigations, Dakin's tubes and the complicated ritual of antiseptics that ornamented military hospitals in 1918 were unused or forgotten. Their place was taken by extensive incisions and plaster of paris splints. Rapid military movements and the need, after the bombing of thickly populated centers, of attending great masses of wounded called more than ever for surgical methods that were rapid and safe and that permitted of prompt evacuation with a minimum of postoperative attention. Trueta has written of these methods in his monograph on the Treatment of War Wounds and Fractures. The interest his manual has aroused is evidence of our concern for military preparedness.

For this reason a few further notes based on experiences gathered during the Spanish Civil War may not be amiss.

Rapidly moving warfare dominated by aviation makes simple surgical methods imperative. The necessity of concealing formations from view from the air and of moving men, wounded and supplies quickly, often under the cover of night, compels economy of materials, space and effort. Supplies and essentials are liable to be scanty or wanting entirely, either because they cannot be brought up or because they have been destroyed. Water, especially hot water, is liable to be short; liquid solutions and glass containers are liable to be spilled or broken. However, one learns to adapt oneself, and as the late Dr. Bethune wrote from China, "I find I can get along and operate as well in a dirty Buddhist temple . . . as in a modern operating room with a thousand accessories." The necessary economy and simplicity may by foresight and preparedness work rather to the advantage than to the disadvantage of the wounded.

PREPARATION

The most satisfactory easily transportable and easily procurable skin disinfectant, both for the surgeon and for the patient, is chlorinated lime.

The surgeon cleans his hands with a cream of chlorinated lime and soda worked well into the skin with a brush. If running hot water is scarce this paste is washed off by having a tiny stream of water trickle

on the hands from an irrigator or a can with a spigot. Cleansing is as thorough as though a much larger stream were used. Following disinfection with lime and soda, alcohol, iodine-alcohol or a mercurial in alcohol acetone solution makes it easier to dry the hands and to put on gloves but is not essential.

The patient is thoroughly shaved, either wet or dry, the hair being removed over the whole area which is subsequently to be encased in plaster. One applies a thick paste of chlorinated lime and soda to the skin of the operative field and removes the paste with moist gauze, working outward from the wound as a center. This really cleans the skin of sweat, mud, dirt and grease; it may then be painted with one of the usual alcoholic antiseptic solutions, iodine or a mercurial.

Draperies should be small, so that the surgeon can keep the field under his eye and watch what unskilled assistance is doing. Large expanses of white sheeting are no guaranty of asepsis but are rather in the way. Four drapes about a yard square clipped or sutured to the skin are enough. The skin edges are further protected by large moist gauze squares. A well constructed metal sacral rest is indispensable; improvisation of boxes and enamel basins is most unsatisfactory, but a fracture table is not essential. Two pairs of small pulleys in the form of a block and tackle arranged overhead with other pulleys fastened to the wall at the foot of the table are just as serviceable and much easier to transport than a heavy fracture table. However, a fracture apparatus such as a Dupuy or Zimmer apparatus makes the placing of Kirschner or Mathews wires easier.

ANESTHESIA

Some form of anesthesia is desirable in which the patient is not entirely unconscious but is able to cooperate to some extent. His cooperation makes transportation to and from the operating room easier and saves work for stretcher bearers, surgeons, orderlies and nurses. Soldiers at the front are notoriously easy to anesthetize; they are usually in good physical condition, not overfed nor alcoholic and, when wounded, are often more or less on the verge of shock, so that a little morphine, a little sedation with barbiturates and a little inhalation anesthesia go a long way toward freeing them of pain.

Thus preparation with morphine plus procaine hydrochloride infiltration around the site of injury is often all that is needed for the accomplishment of a thorough débridement and reduction of a compound fracture.

Plexus anesthesia is very satisfactory for injuries of the upper extremity. Twenty cc. of 1 per cent procaine hydrochloride plus two drops of 1:1,000 epinephrine are injected just above the middle of the clavicle; the needle is pointed toward the spinous process of the first dorsal vertebra. As it strikes the plexus, the man feels a sudden tingling pain in the fingers. One should inject the full amount of procaine solution as soon as this pain is felt, moving the needle about a little to inject the various cords of the plexus. Anesthesia follows almost immediately. If the needle misses the plexus it strikes the first rib; it should be moved about until the plexus is found. If injection is made not squarely into the plexus but around it, anesthesia may take from fifteen to twenty minutes to develop. The interval may be used to attend to other wounded.

For lesser injuries, injection around the site of injury is all that is needed.

A little ethyl chloride inhalation given when all is in readiness is sufficient for the few minutes needed to amputate a mangled arm through the site of fracture;

the man wakes up immediately, may often walk to his bed, travel seated in an ambulance and can be given hot drinks without nausea and vomiting. It is especially important that deep general anesthesia be not used for injuries of the upper extremity, for thoracobrachial plaster of paris is easy to apply if the man is seated but difficult or impossible if he is lying unconscious on a table.

For fractures of the lower extremity, low spinal injection of 100 mg. of procaine hydrochloride dissolved in 3 cc. of spinal fluid injected while the man is seated with one or both legs hanging over the edge of the table produces an ideal anesthesia. The injured man retains the use of his arms and can help balance himself on a pelvic support while plaster is being applied. Evipal or pentothal sodium injected slowly until a light narcosis is reached is satisfactory for men who are shocked or frightened. By injecting the drug slowly, drop by drop, one can maintain a constant light narcotic level. Evipal, however, is not satisfactory in skull injuries with unconsciousness and delirium. It seems to increase the delirium and makes the wounded more unruly.

Ethyl chloride administered by dropping it, not spraying it, on an open face mask is a most satisfactory anesthetic for short maneuvers requiring good relaxation. At the moment when the patient first goes under the anesthetic, when he takes a few deep sighing respirations, the mask should be slightly lifted to allow room for plenty of air. If this is done and sudden inhalation of highly concentrated ethyl chloride vapor is thus avoided, the anesthetic is safe: there is no excitement stage and no struggling, which to wounded with fractures are harmful; relaxation is perfect, and consciousness returns without nausea or vomiting a few minutes after the anesthetic has been stopped. No other inhalation agent seems to meet all requirements for short anesthesia so well. Five minutes is to be regarded as the maximum duration of ethyl chloride anesthesia; if more prolonged narcosis is likely to be needed, ethyl chloride should not be given or anesthesia should be changed to ether. Bulky apparatus, inflammability and the need for expert anesthetists preclude the wide use of gas in advanced hospital formations.

X-RAY EXAMINATION

It is seldom necessary to take an x-ray film of a compound war fracture before débridement. Inspection of the limb before operation and of the fracture during operation usually give the needed information. Foreign bodies and the position of fragments are usually self evident in the course of a proper débridement. It is seldom necessary to take an x-ray film immediately after operation and immobilization if the operation is properly done and splints are properly applied. Radiography at the front is time consuming and cumbersome, fluoroscopy still more so.

The time and place for x-ray examination is at the evacuation hospital and farther back, at a time when fractured bone ends may have slipped or osteomyelitis and sequestration may be demonstrable.

The mobile surgical unit which I headed in Spain was equipped with a good modern portable x-ray apparatus and a dark room included in a mobile unit on wheels. They were not once used. The same was true of other advanced units which I had occasion to observe.

Conceivably radiography and fluoroscopy might be advantageous for chest wounds with suspected intrapleural foreign bodies or for abdominal wounds. It is

questionable, however, whether its limited application in small advanced hospital formations calculated for rapid movement and intense activity justifies the time, weight, bulk and personnel needed for its management.

POSITION ON THE OPERATING TABLE

For injuries involving the front and sides of a limb, the wounded are placed on their back; if both front and back have to be dealt with, the limb is elevated or suspended so that the posterior surface is accessible. The man may also temporarily be placed on his side, but the fracture is likely to be considerably displaced in this position.

The arm may be placed on the operating table at the side of the wounded or laid across the chest; it may be held suspended from a pulley or abducted on an arm board or on a side table. It should be placed in the position in which final reduction is likely to be most easily accomplished and maintained. Draperies should not be so bulky that the fracture may be displaced by their removal; they should allow access to the arm and hand so that slings and pulls may be applied for maintenance of position while the limb is being splinted. The same consideration holds good for fractures of the lower extremity. The patient lies on his back; if the posterior surface of the limb is injured it may be placed in a Böhler frame or held suspended by slings and pulleys to allow access from underneath. In any event slings are best laid under the limb before débridement is begun so the fracture may not be displaced later.

In amputation much blood can be saved and the tourniquet dispensed with if the limb which is to be amputated is suspended vertically upright from an overhead pulley by a clove-hitch passed around the ankle or the wrist. All its venous blood is returned to the circulation in this position, while with a tourniquet, however quickly and efficiently it may be applied, some venous stasis occurs while it is being tightened and the venous blood in the limb is lost.

DÉBRIDEMENT

After everything is properly prepared and in readiness and not before, operation is begun; shaving should be complete, draperies adjusted with a view to their subsequent removal, slings and traction apparatus applied or laid under the limb ready for application; for it should be remembered that after débridement the soft parts and bones are to lie in the position which they are to maintain during healing. It is distressing both to the wounded and to the surgeon to see the limb jostled and moved during the application of retention apparatus, splints and bandages often to an extent that should call for a new débridement before the plaster is finally applied. A tourniquet usually makes accurate inspection and operation easier. It should be used only if it can be rapidly and efficiently put on. It can be kept from slipping down on the limb by a towel clip through the skin or one or two sutures. A pneumatic sleeve is the best tourniquet for the arm, a wide rubber tube or an Esmarch bandage for the thigh.

Everything being in readiness, local, spinal or general anesthesia having been induced, the skin edges are excised in the classic manner, retractors are inserted and held gently but firmly, devitalized muscle, contaminated bone chips, foreign bodies, missiles and pieces of clothing are removed. Special attention is paid to visible shreds of clothing and dirt. The position of the limb on the operating table is likely to differ greatly from that which it had when the missile struck it. Contaminated particles may be dragged up and down from

a line drawn between the wound in the skin and the fracture; soft parts, muscle and fascia may have slid one over the other, occluding the tract. In order to lay all of these recesses wide open, the skin and fascia should be widely incised so that the recesses are not under tension and forcible retraction is not necessary to expose them. If forcible retraction is necessary at the time of débridement, the wound will be under tension later. Wide incisions into skin and fascia are unimportant and can be repaired perfectly; insufficient ones are very important and will determine future loss of the limb, sepsis, spreading osteomyelitis, gas gangrene and phlegmons of the soft parts. If the unimportant superficial structures of the skin and fascia are widely incised, more important deeper structures, muscle and bone, will be spared.

The wound should not be dabbed, rubbed and prodded with gauze sponges. If vessels bleed and it is necessary to use gauze in order to see them, the wound should be firmly compressed with a piece of flat gauze held in the fingers; the gauze should then be slowly rolled back until the bleeding point can be seen and caught with a hemostat. Wiping the wound with gauze makes it bleed more and wipes dirt into its crevices.

Necrotic and contaminated muscle should be excised; severed and contaminated nerve ends may be freshened and brought together with a single fine black silk suture left long and allowed to hang out of the wound if it is thought that suppuration is inevitable, or cut short if it is thought that the wound may heal. Formal accurate perineural nerve suture is rarely indicated.

Severed vessels should be caught and tied. Arterial suture is almost never possible or permissible. A compound fracture with a cold pulseless limb calls for amputation unless exceptional vigilance is possible during the first few days after injury.

Tendons lying in a contaminated area may be allowed to remain if they can be cleaned and covered by clean viable soft parts not under tension. If they are severed, their clean freshened ends may be approximated by a single suture and similarly covered. If it is not possible to cover them they had better be allowed to retract into their sheaths, for if they remain exposed in a wound they will certainly slough. More of them will be saved for secondary suture later if they are allowed to retract.

Open and exposed joints should be similarly covered. If it is possible to sew clean synovia over them without tension, their function may be preserved, but in no case should they be covered by skin sutured under tension.

Entirely loose fragments of bone should be removed. Grossly contaminated bone ends from which the periosteum has been stripped should be removed with the rongeur until clean covered bone appears. Grossly contaminated periosteum should be removed.

If the bone ends hold their position without internal fixation, so much the better. If they tend to slip they may be held by a wire passed through drill holes if it is possible to drill the holes without stripping the periosteum and traumatizing the fracture by dislocating its ends from the wound. Oftener it may be possible to grasp the bone ends and hold them approximated with a towel clip, which should be left in the wound. If its branches cannot be closed, the handles may be tied together with a piece of silk or twine. Only if a bone is widely exposed and will obviously sequestrate is it permissible to use metal plates, which should lie fully exposed in the surface of the wound. Their application in the depths of a wound entails needless trauma and exposure of the bone.

Whether packing should be placed about the fracture depends on the extent and duration of contamination and the completeness of débridement. More or less sequestration will almost certainly ensue if the fracture is surrounded by gauze packs. If it is possible to surround it with soft parts without tension, it may heal without suppuration.

A few sutures are permissible when it seems expedient to cover vulnerable structures—tendons, cartilage, blood vessels—which die when exposed or which it is dangerous to allow to remain so. Such sutures should be of fine 00 or 000 catgut or fine silk (if the operator is incorrigibly silky) and should not create tension. If liberating incisions cannot loosen the parts to be sutured, suture had better be withheld.

If all structures lie perfectly loose and naturally, packing may be omitted. If contamination of the fracture site is such that the wound must be left unclean, it may be better to introduce a pack of iodoform gauze or plain gauze. In any event, it seems, in the light of newer experience, that it may be wise to sprinkle the wound liberally with sulfanilamide powder.

During the whole operation, which frequently it does not take as long to perform as it does to tell about, instruments should be changed or wiped and cleaned constantly with moist gauze. This applies especially to scissor blades and the teeth of tissue forceps. The gauze should be discarded each time, and no sponge or gauze should be introduced into the wound twice. Ample incision into the skin and easy exposure will make débridement, even of extensive wounds, not too time consuming.

SUTURE

After each débridement the question arises "Shall the wound be closed by suture?" The answer is usually like Thackeray's to the young man about to marry: Don't. If the pros and cons are weighed each time, the cons will so outweigh the pros that there will be little doubt what to do. The pros reduce themselves to the advantage of a small linear scar—a negligible advantage. Shortening of time of hospitalization scarcely comes into question, for even though the wound is left open and allowed to granulate it will be closed or may be closed by secondary suture or skin grafting by the time the fracture is consolidated. The cons are overwhelming, for it will rarely be possible, in spite of the promptest and most complete débridement, to assure asepsis in extensive war injuries that warrant the performance of a débridement at all. And if such wounds are closed by skin suture producing even the slightest tension, danger to life and limb is great. In the best of events, if suppuration ensues, hospitalization will be measured in terms of years instead of months. Exception may be permissible in wounds of the hand, wrist and ankle, when the danger of serious sepsis is not great, when the skin can be approximated without tension and when valuable tendons will slough unless they are covered.

The wound is covered with small dressings of sterile gauze and the limb is immobilized for evacuation. In wounds that are likely to bleed, sterile gauze is preferable to Orr's petrolatum pack; wounds covered with petrolatum ooze and bleed much longer than when covered by sterile gauze.

APPLICATION OF PLASTER SPLINTS

The use of plaster of paris may justify a few generalities. In surgery, as in every other art, each material calls for its own technic and what is valid for one medium may not be so for another.

In the United States plaster of paris is used on crinoline or starched gauze bandages; in Spain and France plain unstarched gauze bandages are used. Crinoline plaster bandages have more body and are easier to apply without wrinkles; however, their starch content delays setting and makes it necessary to use rapidly setting plaster of high quality (alabaster or dental plaster) if the cast is to set reasonably quickly. The casts are probably not quite so hard but are tougher than the ones made with unstarched bandages. Plaster on plain unstarched gauze is somewhat more difficult to apply smoothly, especially for those used to starched bandages; however, it sets more quickly without the starch, so that slower plaster of inferior quality can still be used satisfactorily. The casts are harder but more brittle than those with starched bandages; they are likely to be a little thicker. In France and Spain flannel cut to a pattern and immersed in a plaster cream is occasionally used. This is especially useful for jackets, body casts and half body casts (plaster shells). It saves time and trouble when properly applied. For general use when good plaster is available the crinoline bandage is probably preferable; if plaster of a poorer grade, and ordinary commercial plaster such as can be bought at most lime kilns, is all that can be had, unstarched plain coarse mesh gauze bandages are better.

Plaster of paris bandages conform to the shape of the body by being molded to it; they have no elasticity and cannot, like gauze or flannel bandages, be pulled or stretched into shape. Their cohesiveness is great; they will not work or slip or stretch. Every crease and every wrinkle in them becomes petrified when the plaster sets and will cause intolerable pressure if it overlies a bony prominence. To pad plaster with absorbent cotton or some such material is to frustrate the purpose of plaster. It will immobilize imperfectly, for the limb will work up and down in its cotton sheath; it will be more and not less likely to cause pressure sores, for it is impossible to mold it accurately to the limb if it is separated from it by an uneven surface, such as that of cotton padding; and lastly and most important the immobilization due to the plaster sticking to the underlying skin is lost, and traction against muscle pull can be secured only by pressure of the plaster splint against flaring surfaces, such as the knee, the ankle, the dorsum of the foot, the heel and the hand below the wrist, instead of being equally distributed throughout the whole limb, as when plaster is applied directly to the skin.

It is obvious that some way of holding a limb must be devised that will keep it in position while the plaster is being put on. It is equally obvious that unless the limb will hold its position by itself, which it will not often do in fractures, its position cannot be retained by the hands of an assistant, for he must let go each time a turn of bandage or a splint is to come between his hands and the patient's skin. Some form of traction is necessary which can hold its place, at least until the plaster hardens, a metal pin, a bandage or some material that can be incorporated into the splint or retain its position under it. It is obvious again that the hands of an assistant do not meet these requirements. Plaster should be applied with regard for what it can do and what is required of it, and (especially in advanced hospitals where the wounded cannot be kept under observation) with more of an eye to what the next few days, weeks and months may bring than with regard to the needs of the moment.

The limb is kept in position by suspending it or pulling on it with bandages which are greased and are incorporated into the cast but are withdrawn before the man leaves the operating table, for they will cause pressure if allowed to remain. Or at times metal pins may be convenient. The need for these will not be great if unpadded casts are used. Traction should not be too forcible if there has been much loss of osseous substance, for a wide gap between bone ends is likely to lead to nonunion. The perfect relaxation of spinal anesthesia increases the risk of wide distraction.

Dressings should be small, just large enough to prevent plaster of paris from leaking into the open wound; they should be held in place by a few small narrow strips of adhesive and not by a bandage encircling the limb; slings should not be too wide; as much skin as possible should be left uncovered for the plaster of paris to adhere to. Painting the area around the wound with compound tincture of benzoin will prevent acne pustules from old wound secretions and help dressings and plaster to stick to the skin.

The plaster should be applied with due regard for the stresses and strains involving both the fracture and the neighboring joints. Lateral strips are laid on first, a few layers at a time, two or three, not more than four. The fit of the cast depends on the neatness and accuracy of these inner layers. They are molded with the hand to the shape of the limb. Creases and folds are removed by notching the strips or removing a V shaped dart, so that the plaster lies perfectly smooth. A half dozen layers or so are laid on and allowed to set a little; reinforcements are added by using shorter strips at the site of fracture or at the joints or by laying on longer strips folded lengthwise. After these longitudinal strips are hard enough to retain their shape and not buckle or dent, they are held in place by a circular bandage one layer only in thickness; no turns or folds are made in this bandage, but it is cut across and started again as soon as it ceases to run smoothly over the longitudinal strips and the limb. Care should be taken that the layers do not accumulate at the bend of the knee and the elbow. It is just here, where pressure is most likely to be harmful, that several layers of circular bandage are likely to overlap. When additional reinforcement is thought necessary, because the man is unusually robust or heavy or because profuse drainage is likely to wet the cast at the site of fracture or because transportation is likely to be long and hard, metal material may be added, but only after the cast is dry enough to resist pressure. If metal reinforcements are added before the plaster is quite set they will dent it and cause pressure points. Cramer splints (wire ladder splints) are particularly likely to do this. The metal, if rationally applied, need be only light and thin. Strips an inch wide cut from an ordinary tin can are just right. They can be bent and molded by hand to fit the cast accurately. If they do this they are stronger than heavier metal which cannot be accurately applied. They are firmly attached to the surface of the cast with a single layer of circular plaster bandage pulled tight. They are placed at the level of the fracture or over joints so that their width resists bending strain; i. e., two pieces at each side of the knee, three or four pieces around a fractured femur, two pieces laterally for leg fractures. If thin aluminum sheeting is at hand this is to be preferred, being pervious to the x-rays. The cast may be made thin in certain spots so that it can break; e. g., it is desirable to put a few spica turns around the hip and pelvis in high

fractures of the leg, but it is not necessary to immobilize the hip. The cast should be thin at the hip so that it can break here. The ankle should be included in casts for fracture of the femur; but, if the cast is thin at the ankle, motion may be preserved.

Suspension strips and especially hitches about the wrist and ankle must be removed before the man leaves the operating room. If the cast inclines to bend or buckle at the point where it is cut for their removal, reinforcements may be added.

Finally, as long as the wounded can be constantly and carefully watched in the same hospital the circular turns may be allowed to remain; if, however, débridement and immobilization are only preparatory to prompt evacuation, before the man leaves the hospital the circular turn should be slit all the way either up the front or the back of the limb and the cast should be wrapped not too tightly with an ordinary gauze bandage. The cast will be less likely to break if it is thoroughly dry before it is slit, if it is possible to wait twenty-four hours, but it should be slit before the wounded man is evacuated, even though it is not thoroughly dry. In dubious wounds it is better not to wrap the cast but to slit it and leave it open. If this is done there need be little fear of constriction or gangrene.

In fractures of the leg the cast is ordinarily applied with the leg lying flat on the operating table; lateral strips are first laid on, as far posteriorly as possible, they are allowed to set, and the circular bandage is then applied. If the leg lies on a rubber sheet the circular turns can be slid under it without lifting it from the table.

Fractures of the femur are put up with the man placed on a sacral rest, his shoulders supported by a box of equal height; the leg is held suspended from overhead pulleys with the knee slightly flexed; traction is made on the ankle by means of a hitch; another sling about the site of fracture keeps the femur from dishing. In the absence of overhead pulleys and in a pinch the femoral sling and the sling about the knee may be held by an assistant who stands on the table, one foot at each side of the fractured femur, facing the patient's feet. He brings the slings about his neck while his back is a little bent; as he straightens up the slings are tightened and the extremity lifted. A thick cotton pad is placed over the abdomen before the plaster is applied to allow for distention.

Fractures of the arm and forearm are put in plaster with the patient seated, on a stool if possible, on the operating table if not. It is almost impossible to put on a thoracobrachial plaster splint with the man lying on his back; hence the need for avoiding ether or prolonged gas anesthesia. The so-called airplane splint, with the shoulder abducted at 90 degrees, is never used. Such a splint, whether of metal or of plaster, works only when the man is flat on his back; when he is up or has his head raised in bed the weight of the splint causes a valgus angulation of the humerus and produces the deformity it seeks to avoid.¹ If transportation is to be comparatively easy, the arm is put up in 45 degrees abduction or less, with the forearm at right angles to the body in the sagittal plane; the cast should include the chest, both shoulders and the arm to the wrist with a turn or two around the hand, in what is known as the Bastos position, after Bastos, formerly professor of surgery at Madrid, now prisoner in a fascist concentration camp. Care should be taken not to tighten the

turns about the chest; before they are applied the man should be called on to blow his chest up. If he cannot do this the lower part of the chest should be padded. The cast may be reinforced by a stick of wood or a Cramer splint leading from the chest to the elbow. It is not easy to apply and, unless it is fairly heavy, is likely to break at the elbow and no great matter. The weight of the forearm sticking out at right angles to the body tends to twist the whole apparatus outward in order that the arm may drop inward. The projecting forearm makes transportation somewhat awkward; the man is likely to be jostled and bumped unless he is seated, when his knees protect the forearm. If, therefore, evacuation is likely to be troublesome it may be better to let the man carry his arm at his side and his forearm across his chest in a sling. Cotton pads are put under the arm and between the forearm and the chest; the sling, arm, forearm and chest are then encircled with a few layers of plaster of paris applied circularly. This position creates an inward rotation deformity of the lower fragment, but it makes evacuation easier, particularly if the man is to lie recumbent, to walk or to stand. The rotation can be corrected later on reaching the base and a Bastos splint applied in correct position. The man should be tagged to this effect when he is evacuated. Evacuation in a 90 degree abduction splint (airplane splint) is torture to all concerned.

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EPIDEMIC MENINGITIS

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In this discussion the term "epidemic meningitis"¹ is applied to all patients suffering from meningococcal infections. It does not include carriers but does embrace instances of meningococcemia whether with or without clinical evidence of meningitis.

The contention is made sometimes that this disease is much more severe in the presence of an epidemic than among sporadic or endemic cases. On the basis of my own experience during a number of years, such a view is not acceptable. It is even quite possible that during an extensive outbreak many patients may suffer from attacks that are not extremely severe. Consequently the case fatality rate may be comparatively low. On the other hand it is not unusual to have admitted to our contagious disease hospitals patients with a fulminating type of infection at a time when there have been few reports of the disease. Under the latter circumstances the fatality rate is generally very high.

The foregoing explanation is descriptive of the situation as it has existed in Chicago. Since 1937 the incidence of epidemic meningitis has not been great compared to the years 1927-1935.² Nevertheless the percentage of severe cases has attained a high level. In this connection I observed several years ago, when serum was given intraspinally, what appeared to be a paradoxical situation. There was a higher death rate

From Cook County (Contagious Disease Department), Municipal Contagious Disease (Chicago Health Department) and Children's Memorial hospitals.

Read in the panel discussion on Some Contagious Diseases before the Section on Pediatrics at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Hoyne, A. L.: Meningococcal (Meningococcal Infection); New Remedy, Arch. Pediat. 52: 418 (June) 1935; The Treatment of Meningococcal Infections, *ibid.* 53: 164 (March) 1936.

2. Hoyne, A. L.: Meningitis, J. Iowa M. Soc. 26: 549 (Oct.) 1936.

1. Howard, N. J., and Eloesser, Leo: Treatment of Fractures of the Upper End of the Humerus, J. Bone & Joint Surg. 16: 1 (Jan.) 1934.

among the patients who were treated early than there was for those who entered the hospital late in the course of the disease. The solution for this occurrence lay in the fact that, as a rule, a prompt diagnosis was established when meningitis was of a fulminating type and as a result treatment, which often proved futile, was

TABLE 1.—*Epidemic Meningitis at Cook County Contagious Disease Hospital*

Year	Patients	Deaths	Lumbar Punctures	Average Lumbar Puncture	Fatality Per Cent
1937	60	18	127*	2.1	30.0
1938	26	2	25†	0.9	7.6
1939	13	2	25‡	1.9	15.3
Total	99	22	177	1.7	22.2

* Includes fourteen punctures prior to admission.

† Includes ten punctures prior to admission.

‡ Includes four punctures prior to admission.

TABLE 2.—*Epidemic Meningitis at Municipal Contagious Disease Hospital*

Year	Patients	Deaths	Lumbar Punctures	Average Lumbar Puncture	Fatality Per Cent
1937	5	2	31	6.2	40.0
1938	13	3	14	1.0	23.0
1939	8	0	9	1.1	0
Total	26	5	54	2.0	19.2

instituted at once. But if the patient suffered less severely and especially if no petechiae were seen, several days often elapsed before a physician was summoned and hospitalization ordered. Perhaps then because of the patient's natural resistance or the type of infecting organism, appropriate measures were successful in bringing about recovery.

Often in the past we feared the outcome for the patient with petechiae. Meningococcemia frequently suggested a fatal prognosis. In many such instances there was little or no rigidity of the neck. Yet even without meningeal signs it was a common practice, and still is in some localities, to make a lumbar puncture and administer specific serum. This procedure was carried out even if the spinal fluid appeared normal and no organisms were found. But after the introduction of serum intrathecally the cell count often increased and meningococci became numerous. The irritative effects³ of the serum caused meningitis to be plainly evident. Stiffness of the neck if not present previously now existed and opisthotonos frequently became pronounced with the repetition of intraspinal treatment. The foreign substance (serum) entering the spinal canal increased the permeability of the meninges, and subsequent withdrawals of spinal fluid fulfilled all expectations for a bacterial meningitis. Then future attention was focused on the contents of the spinal fluid. It seems to me that there is often too much anxiety regarding the spinal fluid while insufficient thought is directed toward the condition of the patient. It is really the patient whom we wish to treat, not his spinal fluid. In 1934 I abandoned all forms of intraspinal treatment and never have had any cause to regret such action.

For several years antedating the introduction of sulfanilamide, the procedure⁴ was as follows: (1) blood for culture from each patient, (2) spinal puncture

deferred for patients with petechiae, (3) diagnostic lumbar puncture for every meningitis patient without petechiae. In each instance an effort was made to estimate the amount of antimeningococcus serum or meningococcus antitoxin that would be required to bring about recovery. Just as with diphtheria antitoxin, dosage was based largely on one's experience. Severity and duration of the disease received primary consideration; age was sometimes a factor. Meningococcus antitoxin was given in doses of from 60,000 units (180 cc.) to 100,000 units (300 cc.). For an infant the smaller dose might suffice. If antimeningococcus serum was selected the dose usually varied from 150 to 300 cc. In either instance the antitoxin or serum was diluted with 10 per cent dextrose in saline solution of at least equal volume but preferably double or more the volume. It is important to have the dextrose in saline solution; otherwise the serum may precipitate. To this mixture from 0.5 to 1 cc. of epinephrine hydrochloride was added. The mixture at body temperature was then ready for administration by the drip method. When this plan is followed the flow should be started very slowly but can soon be increased to at least 60 drops a minute. If there is not marked improvement within twelve hours, the treatment should be repeated. By this method I have given as much as 1,200 cc. of horse serum (antitoxin) within four days and seen the patient make an excellent recovery without complications.

In 1935⁵ for seventy-six consecutive patients with meningococcic meningitis treated at the Cook County Hospital and Municipal Contagious Disease Hospital the fatality rate was 11.8 per cent. All these patients were treated intravenously in the manner described without intraspinal therapy. In another group of fifty-four patients similarly treated the fatality rate was 9.2 per cent and the rate for thirty-six of that number who were 20 years of age and less was only 2.6 per cent. At Children's Memorial Hospital the laboratory

TABLE 3.—*Epidemic Meningitis at Children's Memorial Hospital*

Year	Patients	Deaths	Lumbar Punctures	Average Lumbar Puncture	Fatality Per Cent
1937	6	1	17	2.8	16.6
1938	2	0	3	1.5	0
1939	1	0	2	2	0
Total	9	1	22	2.4	11.1

One child died in admitting room ten minutes after entering; this patient not included.

TABLE 4.—*Epidemic Meningitis at Three Hospitals: Combined Tables*

Year	Patients	Deaths	Lumbar Punctures	Average Lumbar Puncture	Fatality Per Cent
1937	71	21	175	2.4	29.5
1938	41	5	42	1.0	12.1
1939	22	2	36	1.6	9.0
Total	134	28	253	1.8	20.8

has reported sterile spinal fluids within forty-eight and seventy-two hours following the administration intravenously of large doses of meningococcus antitoxin. In each instance a prior culture had been positive. These results are not cited with the thought that intravenous serum therapy should be used to the exclusion of sulfanilamide. They are presented for the purpose of

3. Hoyne, A. L.: Meningococcic Meningitis: Importance of Intravenous Therapy, Illinois M. J. 68: 307 (Oct.) 1935.

4. Hoyne, A. L.: Intravenous Treatment of Meningococcic Meningitis with Meningococcus Antitoxin, J. A. M. A. 107: 478 (Aug. 15) 1936.

5. Hoyne, A. L.: Treatment of Meningococcic Meningitis Without Intraspinal Therapy, Nebraska M. J. 21: 321 (Sept.) 1936.

emphasizing that those who depend solely on the use of sulfanilamide for the treatment of epidemic meningitis are not injecting an irritative serum into the intrathecal sac. This fact receives scant thought when spectacular results are attained by the administration of sulfanilamide by mouth or subcutaneously. To me

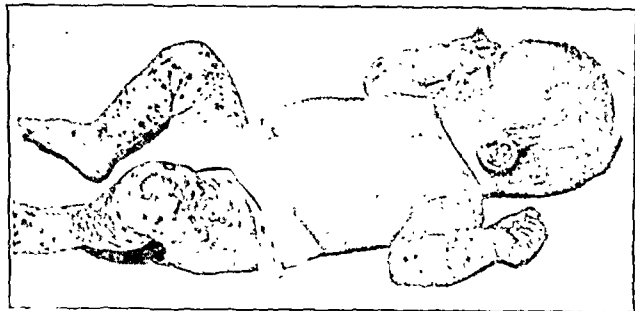


Fig. 1.—Child in coma, petechiae numerous, on April 27, 1938, fourth day of disease.

it is an extremely important factor in sulfanilamide treatment when the drug is given in the customary way. In the contagious disease hospitals in Chicago and at Children's Memorial Hospital, no intraspinal therapy is adopted for any kind of meningitis patients. Eventually, I believe, no one with experience will administer serum intrathecally.

From 1937 to 1939 inclusive ninety-nine meningococcal patients were treated in the contagious disease department of the Cook County Hospital, Chicago. The ages varied from 6 months to 62 years and the total number of deaths was twenty-two, or a fatality rate of 22.2 per cent. These figures include all patients regardless of how soon death occurred following admission. Of the entire group, twenty-seven patients were treated exclusively with meningococcus antitoxin, twenty-two with standard antimeningococcal serum, fifteen with sulfanilamide and two with sulfapyridine. The remainder received various combinations of serum, antitoxin and sulfanilamide. There were only three patients who

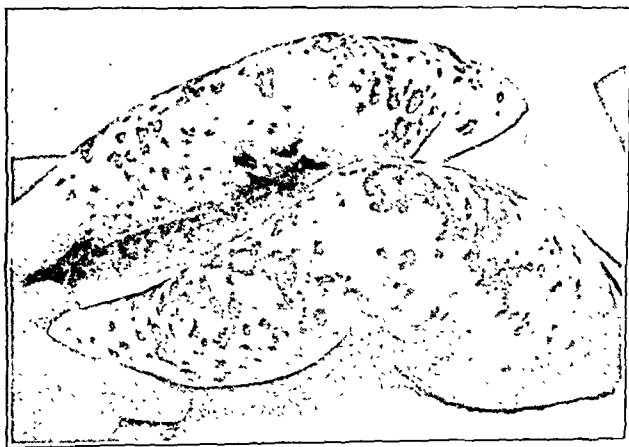


Fig. 2.—Close-up of figure 1, showing massive purpuric eruption of legs.

had any intraspinal treatment. Two of these were given this form of therapy prior to admission. All three are included among the deaths. From September 1937 to March 1938 there were twenty-eight consecutive patients without a death. During the same years there were sixteen patients treated without any lumbar punctures. In each instance the diagnosis was confirmed by

blood culture. In the latter group there were two deaths. Patients with meningococcemia and little or no evidence of meningitis sometimes do better when no intrathecal punctures are made. Within the past few years we have treated approximately forty patients in this manner.

Even though the meningococcal patient has both clinical and bacteriologic evidence of meningitis, frequent lumbar punctures for the purpose of drainage are not required. In fact, one's aim should be to make as few punctures as possible. One lumbar puncture when necessary for diagnosis is often sufficient. No permanent benefit is derived by making numerous taps with the object of relieving intracranial pressure. With each



Fig. 3.—Bright appearing baby with petechiae fading on May 4, eleventh day of disease, one week after intravenous treatment.

successive puncture the quantity of spinal fluid withdrawn is likely to be greater unless a block occurs, which is less likely to happen if there has been no intrathecal treatment. Frequent drainage is more apt to promote hydrocephalus than to prevent it. The fewer the punctures, the fewer the hospital days. Most of our patients are well in less than two weeks.

In the accompanying tables 134 meningococcal patients are enumerated. They were divided among three hospitals and for the most part treated in the manner described. The number of lumbar punctures in relation to the recovery rate for the different years is a matter of interest, though not necessarily significant. None of the surviving patients developed any serious complications after treatment was commenced. There was only one recurrent case. This was a man treated exclusively with sulfanilamide and whose recovery had appeared to be complete. None of the patients were given any opiates. Among the 134 patients there

were seventeen 1 year of age or less and only two deaths in this group. There were eleven patients more than 35 years old with three deaths. The fatality rate for all 134 patients was 20.8 per cent.

No detailed description of sulfanilamide treatment seems necessary here. Its great value is unchallenged but in many instances an initial dose of serum or antitoxin intravenously seems well worth while. Intravenous therapy then may be followed by the administration of sulfanilamide orally.

REPORT OF CASE

An example of what may be accomplished without intraspinal therapy is illustrated by the case of V. L., an 8 months old boy:

The baby was admitted to Children's Memorial Hospital on the first day of his illness. A lumbar puncture, which might properly have been omitted, disclosed a clear spinal fluid under normal pressure with a count of 10 cells, mostly lymphocytes. No organisms were seen on smear but the culture was positive for meningococci. The blood culture was also positive, and gram-negative organisms were isolated from lesions in the skin. The temperature ranged between 99 and 106 F. during the first three days. A total of 120,000 units of Ferry's meningococcus antitoxin was given intravenously within the first five days. Small doses of sulfanilamide, from $2\frac{1}{2}$ to 10 grains (0.16-0.65 Gm.) every four hours, were also administered intermittently for twenty days.

A second lumbar puncture was made on the twenty-fourth day of illness. In this instance the spinal fluid was also clear. The cell count was 9 and the culture (at the end of forty-eight hours) was negative. Results of the two lumbar punctures are convincing proof that no intrathecal taps were required.

Photographs taken on the fourth and eleventh days of the disease are indicative of the rapid progress toward recovery after intravenous treatment. There were no complications other than scarring at the sites of the cutaneous lesions.

SUMMARY AND CONCLUSIONS

Intraspinal therapy is to be condemned and the intravenous route advised if an antiserum is used.

Fifty-four patients with a fatality rate of 9.2 per cent were treated exclusively with antitoxin intravenously.

Spinal puncture may be necessary only for diagnosis. Frequent lumbar punctures for drainage are not to be advocated.

Approximately forty patients were treated without any intrathecal punctures.

The success of sulfanilamide therapy is to be attributed in part to the fact that ordinarily no intraspinal treatment is administered.

Permanent benefit for the relief of intracranial pressure by means of spinal fluid withdrawal is questionable.

Antitoxin or serum and sulfanilamide combined is recommended for superior treatment. Good results may be obtained with either one alone without intraspinal therapy.

Advantages which may be expected from the treatment of meningitis without intraspinal therapy are lower fatality rates, more prompt recoveries, few, if any, lumbar punctures required, minimized complications, opisthotonos rare, blockage problems unusual, intracranial pressure signs not observed as frequently as when numerous punctures are made for withdrawal of spinal fluid, discomfort and pain diminished, secondary infections as a result of many spinal taps eliminated, chance of injury to intervertebral disks reduced, hospitalization time shortened and recurrence of infection seldom observed.

25 East Washington Street.

THE TEN COMMANDMENTS FOR THE TREATMENT OF COMPOUND FRACTURES

JAMES E. M. THOMSON, M.D.

LINCOLN, NEB.

Increasing interest in this important subject is evidenced by the recent frequent contributions to medical literature. What was learned from the last World War, plus the increasing number of casualties from modern transportation, farm and industrial accidents, has made possible a clear conception of what is demanded in the way of treatment for compound fractures. The fact that perhaps more than 95 per cent of compound fractures are given first aid by laymen and surgical attention by general practitioners rather than by orthopedic and fracture surgeons presents an important challenge to these specialists to maintain constant refreshing interest essential to insure the general application of the basic principles of treatment, not only among physicians but among first aiders as well. Too often first aid and initial medical treatment is inadequate and responsible for unnecessary secondary trauma to an extremity. In other words, it is the man who attends the case in the first six to ten hours who determines the success or the failure of treatment. The specialist gets the wreckage for salvage.

The difficulty in standardizing methods is the fact that each compound fracture offers a different problem from every other compound fracture, sufficient to tax the judgment of the best trained surgeons. No single program or procedure is adaptable in all cases. Elbert H. Caldwell¹ aptly comments "The result of any procedure depends as much on the surgeon and his application as on the merits of the procedure." There are, however, virtues in almost every procedure that might be applicable under certain circumstances. Therefore, to treat compound fractures one must be broad minded and honest but critical in one's judgment and evaluation of procedures and apply them as the need arises.

The objects of treatment should be² (1) to care for the general condition of the patient, (2) to obtain healing of the broken bone with the best possible alinement of fragments and the least possible impairment of function and (3) to prevent or control infection. Therefore any recommended procedure of treatment for such serious and potentially serious injuries as compound fractures should comprehend every phase that would in any way favorably influence the outcome of the case.

Purely for the sake of impressing myself with the importance of a routine procedure to follow in the treatment of compound fractures, I have called my rules "the Ten Commandments for the treatment of compound fractures." Not like the original commandments, however, which have stood the test of time, these commandments have been changed with our changing ideas and methods; but in the main they have served as a constant reminder against omission and commission. Every commandment will not apply to every compound fracture, but good judgment and experience will check out the unessential.

Read before the Section on Orthopedic Surgery at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Caldwell, E. H.: The Treatment of Compound Fractures, *Arch. Surg.* 35: 368 (Aug.) 1937; *Am. J. Surg.* 43: 554 (Feb.) 1939.

2. Darrach, William: Compound Fractures, *Arch. Surg.* 40: 821 (May) 1940.

FIRST COMMANDMENT.—*Splint and immobilize a compound fracture at the scene of the accident and transport the patient with celerity and great care to a hospital adequately equipped for treatment.*

It is deplorable that the first step is usually carried out by laymen who are inexperienced and overzealous well wishers and that the average ambulance called is unequipped or the physician who is summoned is untrained to meet this situation. The work of the various organized fracture committees has scarcely scratched the surface in stimulating in the minds of the populace the importance of this vital commandment in regard to first aid care and the relation that it bears to the ultimate end result. Much more can be done in the way of education along this line.

Although the patient may not exhibit apparent evidence of shock as he lies by the ruins of an overturned car, this is a potential complication of every severe compound fracture. Therefore it is important to keep him warm and protect him from the elements while waiting for an ambulance or physician. The protection of secondary trauma during transportation is best prevented by adequate 'splinting where he lies,' with Thomas (for lower extremity injuries) and Murray-Jones (for upper extremity injuries) splints in the approved manner. If these are not available, wooden splints, taking in the joints above and below the site of fracture, are acceptable. Gentle handling is most important. If the compounding is from within, outward traction is less desirable, as there is always the possibility of carrying contamination into the depths of the wound. However, with early débridement it is not of vital importance that a first aider diagnose and distinguish whether the compounding is from within or from without. The important thing, after all, is the immediate immobilization with moderate traction and the rapid transportation to a hospital where adequate care can be given. The most that should be done to the wound is the application of a sterile dressing, if available. A tourniquet or hypnotic may be necessary as an immediate first aid measure.

SECOND COMMANDMENT.—*Make an emergency case out of every compound fracture, giving the earliest possible adequate treatment.*

Admission to the hospital should imply emergency attention in the operating room and an x-ray examination with a portable machine. Minutes and hours must be economized for success. Prompt cooperative efforts among the surgical, resident, operating room and x-ray staffs are absolutely essential. I believe that the only exception to this routine is when the severity of the injury is such that shock is, in the experienced judgment of the surgeon, such a complicating factor as to warrant delay for resuscitative measures. It often pays to wait long enough to give 1,000 or 500 cc. of 5 or 10 per cent dextrose solution, or even a transfusion, than to subject a shocked patient to a long anesthetic and a surgical procedure. Usually an hour or two at the most after arrival at the hospital is sufficient for such resuscitation. In cases of severe compound fractures of the bones of children and of elderly persons, the potential factor of shock makes delay for restorative measures of major importance. Those in the extreme age groups are more susceptible to shock than the adult in the in between group and should be given the greatest consideration.

However, the chances of eliminating infection are reduced with each hour of delay. From six to ten hours after the accident, infection has gained a foot-

hold in the tissues and is hard to combat. Examination, palpation and manipulation, which lend themselves to unnecessary roughness and possible secondary trauma, are to be avoided. Inspection and x-ray examination should prove sufficient to justify sound judgment and decision with respect to a suitable *modus operandi*. When the splints are removed the position and traction should be maintained on a fracture table or other traction apparatus. A general anesthetic is usually preferable.

THIRD COMMANDMENT.—*Scrub the limb about and away from the wound with green soap and flowing sterile water for ten minutes.*

After the patient has been anesthetized, the splint removed and traction established by manual holding or by a traction device on a fracture table, a dry shave should start preparation of the extremity. With sterile hands and scrub brush the surgeon continues the preparation of the extremity by scrubbing with green soap and a stream of flowing warm sterile water from an elevated jar through a sterile tube. The water should drain away from the wound, which should be protected by frequent changes of dry sterile gauze dressing. (Ether or benzine may be used to remove grease from the skin.) Next the wound itself is superficially irrigated with warm water or physiologic solution of sodium chloride and the foreign material and clots allowed to be washed out. A sterile gauze dressing is placed on the wound and the cutaneous surface is painted with a mild antiseptic (merthiolate, metapen or weak tincture of iodine). The area is now draped in the conventional manner.

FOURTH COMMANDMENT.—*Debride every wound thoroughly with proper respect for anatomic structures and close those wounds which experienced surgical judgment seems to justify.*

No matter how small the wound, and whether from within or from without, conservative, intelligent débridement carries a tremendous influence in obtaining a clean wound. A puncture wound may carry clothing, leather or dirt into the bony fragments. Even though the wound is separated from the fracture by muscle or fascia, if infected material is carried in, the fragments may ultimately be involved. The added trauma of débridement and cleanup to the skin and superficial soft tissues of the underlying area will in no wise influence primary healing. An understanding of what constitutes a thorough débridement is essential. The operator, with a sharp scalpel, should start at a point farthest away from the dependent portion of the wound and remove not only the cutaneous edge but also attached injured and devitalized tissue. Next, clots and foreign material are picked out; devitalized, lacerated muscle tissue and shreds are removed by sharp dissection. A constant stream of warm sterile physiologic solution of sodium chloride aids in cleaning out the debris and in pointing out, by freshening the structures, further injured tissue shreds to be removed; bleeding points can be spotted and injured nerves and tendons identified. As the bleeding points are spotted they should be tied off but should not be roughly grasped by forceps with a mass of muscle, as this will strangulate the area clamped and leave a fertile medium for bacterial propagation. Severed nerves and tendons should be repaired, and even major blood vessels when possible. One might add another commandment: "After débridement, do not swab or pour into a wound any strong astringent antiseptic, as it coagulates and further devitalizes fresh tissue, thereby making a clean wound virtually a classic

medium for bacterial invasion." I would not consider such a procedure appropriate in performing a tendon transplant or herniotomy. If one is not satisfied with the thoroughness of the débridement and salt solution cleansing, no damage seems to be done by irrigating the wound with an aqueous solution of merthiolate; however, vigorous swabbing should be avoided, as it stimulates bleeding, which should have been arrested.

Small wounds, which comprise most compound fractures, are usually of the "from within out" type and can be closed after conservative débridement; but rare surgical judgment and long experience are needed to know which of the severe wounds can be safely closed with a reasonable expectation of not having infection develop. However, I close loosely almost every wound if it can be done without putting the tissues under too much tension. In two instances plastic shifting of flaps has proved successful with superficial lateral slits to insure against stretching; but such ventures are seldom indicated and should be performed with grave apprehension as to their outcome.

FIFTH COMMANDMENT.—*Reduce, after débridement, every compound fracture and firmly fix the fragments in place.*

Here, I believe, lies the secret of more often obtaining union, even in spite of infection, and also of obtaining a better functional result. It has long been a recognized fact that improper alinement and apposition, and inadequate fixation of bone fragments, form a most reasonable cause for delayed or nonunion with or without infection. This fact is just as true in simple fractures as in compound fractures. It is particularly essential that an adequate reduction be obtained, since compound fractures already communicate with the outside world. Immobilization may be accomplished by means of wires or pins above and below the fracture which, when embedded in casts or splints, frequently stabilize the reduction and prevent loss of position. Often accurate impingement of the reduced fragments furnishes sufficient internal fixation. However, none of these methods give the rigid fixation essential to promote early healing of the fractured fragments of long bones. Slight movements may injure the granulations and osteogenic reconstructive processes and may thereby open new fields for bacterial invasion. Metal plates, screws, wires and nails have been used in the field of compound wounds and also, when possible, have been inserted through incisions away from the compound wound. More recently stainless steel plates have been successfully used. Certain of these metals do not corrode, nor are they affected by body fluids (Sherman,³ Darrach²). When the plates used are of the same stainless metal as the screws there is no electrolytic or tissue reaction; they hold tight and do not seem to influence infection when present. When they have served their purpose they can be removed. Our experience with metal fixation of compound fractures has been limited to vitallium plates and screws, which I believe, as does Willis C. Campbell,⁴ furnish a perfectly adequate means of rigid fixation; their use is warranted more often than it is employed. The reports of Venable and Stuck⁵ with regard to the inertness of vitallium in the tissues have been substantiated in my modest clinical experience not only in simple fractures

but in compound fractures as well. I now use it nearly always in every case of compound fracture in which rigid fixation is necessary in maintaining reduction, particularly when there is considerable comminution. However, one who attempts such measures in surgery must be master of the most meticulous surgical technic. Not only must he stock the various sizes and types of plates and screws and have the proper tools with which to handle the fragments, plates, screws, nails, wires and pins but above all things he must have profound experience and knowledge of how to use them. These procedures should be done with the minimum amount of trauma to the fragments and soft tissues and should never be attempted by the occasional operator on fractures. Unless a man is constantly doing this kind of work he has absolutely no business fooling with internal fixation.

SIXTH COMMANDMENT.—*Coat the wound with crystals of sulfanilamide and give sulfanilamide or its derivatives orally as indicated.*

The use of sulfanilamide in compound wounds was called to my attention early in 1938 by J. Albert Key⁶ in referring to the then unpublished work of Jensen, Johnsrud and Nelson.⁷ I have followed similar measures in every compound fracture since and feel that, although sulfanilamide may slow primary wound healing slightly, it has a markedly deterring effect on local infection. I always accompany this by the oral administration of sulfanilamide or, when this is not tolerated, deep muscular injection is used in adequately prescribed therapeutic doses. Occasionally I use it orally and hypodermically, as does Campbell,⁴ in the preoperative and postoperative care of certain extensive reconstructive operative procedures in which there is a potential possibility of lighting up latent infection, with equally gratifying results. Crystals are also used as a thick dusting powder over small punctured wounds after débridement or over sutured closure of compound fractures. I realize that the fifth and sixth commandments offer exceedingly controversial ideas and recognize the fact that sufficient experimental work has probably not been done to justify such empiric use of this drug as a prophylactic measure, but my clinical experience has seemed to warrant its continued use in surgery in the manner described. Should one's judgment with regard to primary closure be wrong and infection develop in the wound, it can be recognized early by the physical and clinical symptoms and inspection of the wound through the fenestrated cast. The stitches should be removed and the wound opened wide and packed with sterile petrolatum gauze (Orr treatment⁸). After long experience with this method since its inception I am convinced that as a dressing in a deep wound which is already infected there is no irrigation used in any other treatment that compares with it. Wounds that are left open owing to extensive loss of tissue or potential infection are coated with sulfanilamide crystals and gently packed with petrolatum gauze. Dressings are changed only when a malodorous condition exists or excessive drainage

3. Sherman, W. O'Neal: The Treatment of Compound Fractures, Arch. Surg. 40: 838 (May) 1940.

4. Campbell, W. C.: Sulfanilamide and Internal Fixation in Compound Fractures, a paper prepared for the 1940 meeting of the American Orthopedic Association, as yet unpublished; also a personal communication.

5. Venable, C. S.; Stuck, W. G.; Beach, Asa: The Effects on Bone of the Presence of Metals Based on Electrolysis, Ann. Surg. 105: 917 (June) 1937. Stuck, W. G.: Electrolytic Destruction of Bone Caused by Metal Fixation Devices, J. Bone & Joint Surg. 19: 1077 (Oct.) 1937.

6. Key, J. A.: The Treatment of Compound Fractures, Nebraska M. J. 24: 367 (Oct.) 1939. Key, J. A., and Burford, T. H.: Local Implantation of Sulfanilamide in Compound Fractures, South. M. J. 33: 449 (May) 1940. Key, J. A.: Effect of Local Implantation of Sulfanilamide in Joint and Other Tissues, read before the American Orthopedic Association, 1940.

7. Jensen, N. K.; Johnsrud, L. W., and Nelson, M. C.: The Local Implantation of Sulfanilamide in Compound Fractures, Surgery 6: 1-12 (July) 1939.

8. Orr, H. W.: Osteomyelitis and Compound Fractures, St. Louis, C. V. Mosby Company, 1929; The Treatment of Compound Fractures, Arch. Surg. 40: 825 (May) 1940.

endangers the immobilized fractures in the cast. With this, of course, oral administration of sulfanilamide is essential.

SEVENTH COMMANDMENT.—*Immobilize compound fractures in a plaster of paris cast, adequately fenestrated for the observation of the wound and surrounding tissues.*

The more rigid the immobilization the better are the chances of avoiding infection and promoting healing not only of the bones but of the soft parts. It is my belief that, although metal splints and mechanical apparatus are extensively used in the larger clinics, where there are many assistants, assistant assistants, fellows, residents, interns and splint orderlies to look after them, they are responsible for many of the subsequent infections, delayed unions and nonunions, because of the fact that they are so often getting out of adjustment and balance, thereby constantly causing movement and irritation to the injured structures. On the other hand, for the surgeon in private practice, without the numberless attendants and assistants that a large clinic offers, a well padded, properly applied plaster cast which immobilizes the joints above and below the site of the fracture is not only the best

TABLE 1.—*Forty-Nine Patients Having Compound Fractures*

Average age	30 years
Oldest	84 years
Youngest	6 years
Ratio of males to females.....	3 to 1

These patients were completely studied, and in this group there were fifty-three compound fractures; i. e., four patients had two extremities with compound fractures.

TABLE 2.—*Location of Compound Fractures*

Foot	5	Patella	5
Leg	25	Thigh	2
Hand	3	Forearm	6
		Arm	7

Nine of these patients also had simple fractures of other extremities, but these simple fractures are not included in this study.

method of immobilization but allows him hours of peaceful rest and satisfaction that he could never obtain if he were harassed by the worries of how the traction and countertraction were holding in every case of compound fracture. The cast should be well padded with felt over the bony prominences, and the entire extremity with sheet-wadding bandage. It should be strong enough to allow generous fenestration over the site of the wound and fracture for constant observation and dressing. If there is any evidence whatever of swelling, the entire length should be split, not only the cast but the padding as well, and the edges spread. However, under ordinary circumstances, when the limb is properly swung up under a Balkan frame and not allowed to assume a position of dependence, one seldom sees sufficient swelling to warrant splitting. However, those without sufficient experience in applying well fitting casts had better be safe than sorry by following the rule of splitting every cast. Constant observation is the rule. Pain, swelling or impairment of circulation, one or all, are symptoms that signify trouble that must be corrected. The rules I follow for the types of casts are: For compound fractures of the hand and forearm the cast should extend from the axilla to the base of the fingers, and farther if indicated, with the elbow flexed at an angle of 90 degrees in supination or pronation, depending on the type of fracture. Fractures of the humerus are placed in an arm and body spica in an

appropriate position of rotation and abduction. Compound fractures below the knee are treated in a cast which extends from the groin to the toes, with the knee appropriately flexed and the foot at a right angle with the leg. All other compound fractures of the lower extremities are treated in a single or double spica cast in appropriate abduction and flexion.

TABLE 3.—*Etiology*

	Cases
Automobile accidents	25
Gunshot wounds	2
Falls (home and at play).....	8
Falls (from pole or tree).....	4
Machinery and occupational	7
Athletic injuries	3
Total	49

TABLE 4.—*Treatment*

	Cases
Attempted closures made.....	33
Primary healing not obtained.....	6
Skin graft used.....	1
Nonunions treated by bone grafts.....	3

EIGHTH COMMANDMENT.—*Give in every case of compound fracture at once a prophylactic injection of antitetanus serum combined with the Bacillus welchii-perfringens serum.*

In a few compound fractures that occur it may not be necessary to take this precaution, but why should one take the chance when there is absolutely no way of being sure that tetanus or gas gangrene may not develop? One minim (0.06 cc.) or so of the serum intradermally a half hour prior to the full injection has prevented any serious serum reaction. With observation of the eighth and ninth commandments I have not (I knock on wood as I write this) had a single case of tetanus or gas gangrene in over five years.

TABLE 5.—*Results*

	Cases
Wounds not closed.....	20
Secondary closure	4
Healed by granulation.....	11
Skin grafts	5
Nonunions	3
Bone grafts for nonunions.....	2

TABLE 6.—*Materials Used*

	Cases
Vitallium plates	6
Plates removed	3
Vitallium screws	2
Vitallium nails	2
Nails removed	1
Taut wire, fixed traction.....	11

NINTH COMMANDMENT.—*Give a prophylactic dose of x-rays twice daily for three or four days over every compound fracture.*

James F. Kelly⁹ has successfully treated many cases of gas gangrene with x-rays and has recommended as a prophylactic dose from 30 to 50 roentgens twice a day for three or four days. I have followed this practice in nearly every case for the past few years, and

9. Kelly, J. F.; Dowell, D. A.; Russum, B. C., and Colien, F. E.; *The Practical and Experimental Aspects of the Roentgen Treatment of Bacillus Welchii (Gas Gangrene) and Other Gas-Forming Infections*, Radiology 31: 608-619 (Nov.) 1938.

as a result I know little regarding this complication except what appears in the literature.^{9a}

TENTH COMMANDMENT.—*Use pectin therapy in all superficial open wounds.*

As petrolatum gauze forms the best dressing for deep wounds, so a 2 per cent aqueous solution of pectin saturated gauze forms, in my experience, the best dressing for superficial wounds. From a scientific standpoint this substance is of unproved value in the treatment of wounds. There has been no sound foundation for the assumption that pectin solution has any bactericidal properties in the wound. I do know that under certain circumstances¹⁰ streptococcus and other pathogenic bacteria do not live in this medium. However, when used as a dressing, 2 per cent aqueous nickel pectin has a profound absorptive and hygroscopic influence which actually licks up superficial pus, secretions and debris and seems to stimulate clean, fresh granulations and peripheral scarring, offering a delightful surface for skin grafting and secondary closure. Further, it is comfortable to the patient. I have also found pectin particularly useful in preparing old burn granulations for skin grafting.

TABLE 7.—*Amputations*

Amputations	2 cases
1. Because of severe lacerations	
2. Because of circulatory insufficiency one year after fracture	
Death	1 case
Due to multiple fractures following automobile collision	

TABLE 8.—*End Results*

	Cases
Good results	35
10% or less disability for occupation	
Fair results	10
10% to 20% disability for occupation	
Bad results	4
20% disability or more for occupation	

CONCLUSION

Just as the Lord's Ten Commandments are never always obeyed, so it is with these ten commandments for the treatment of compound fractures. I have not always followed these principles completely. There are times when they will not all apply. They simply furnish a standard set of rules to follow for guidance. My idea has been that by using them I seldom overlook a single factor which might contribute to the better functional end result. I realize that I do some things that are not generally approved or well founded. However, I am convinced that they apparently do no harm but seem to contribute to fewer complications and better end results. I feel sure that if every surgeon treating fractures would set up a complete procedure covering every phase or possibility connected with the treatment of compound fractures and have his staff follow it implicitly for five years he would find that his results for that period would be far superior to any similar previous period. The statistical information with respect to a study of my last forty-nine patients who have had compound fractures is given in the tables.

1307 N Street.

9a. AUTHOR'S NOTE. My attention has been called to the danger of combining x-ray and chemotherapy in the treatment of gas gangrene. It is apparent that a choice must be made of one or the other in each case. However, we have noted no ill effect from their use as prophylactic measures where smaller doses of x-rays and sulfanilamide are used.

10. Haynes, Edith; Tompkins, C. A.; Washburn, Grace, and Winters, Matthew: Bactericidal Action of Pectin, *Proc. Soc. Exper. Biol. & Med.* 36: 839 (June) 1937. Pectin as an Antiseptic, current comment, *J. A. M. A.* 109: 1283, 1937. Thomson, J. E. M.: Pectin in the Treatment of Infected Wounds, *Industrial Med.* 7: 441 (July) 1938.

ABSTRACT OF DISCUSSION

DR. ROBERT W. JOHNSON JR., Baltimore: Dr. Thomson has covered almost all the sins of omission and commission that the surgeon can fall into in dealing with compound fractures. I have found that students are leary of a decalogue or other Biblical reference and I have condensed my admonitions to them in an alliterative manner into five principles: splinting, shock, surgery, sulfanilamide and serum. They seem to remember that, and I was pleased in looking over the examination papers a few weeks ago to find that I did not have to fail any one on the question of how to deal with a compound fracture of the femur from the moment of onset to six months after it had occurred. I want to point up Dr. Thomson's admonition in the first commandment to avoid undue speed in the transport of the patient to the hospital. Prompt action is necessary but bumpy handling is bad. In the third commandment I particularly liked his emphasis on the use of plenty of running water as a cleansing agent and also in the use of that same agent mechanically irrigating the wound during the surgical process of débridement, and also his insistence on the avoidance of astringent antiseptics in and around the wound. I find some reason to add caution to his suggestion that fixation plates be used in all compound fractures. He does qualify it, but a great many fractures are treated in hospitals where it is difficult to get adequate assistance and where adequate supplies are not available, so I think that his caution with regard to that should be emphasized because plating a fracture without adequate assistance is no easy job and certainly prolongs shock and trauma if it is not done properly. With regard to sulfanilamide, I am for it from the ground up, but I have used it only by mouth rather than in the wound itself. We have in sulfanilamide a unique agent which acts through the blood stream as a deterrent of infection; the use of it in the wound perhaps should be further checked, despite the enthusiastic reports that have come from a number of sources. I should like to add a point which is important: Fractures, in small communities especially, should all be in the hands of a single surgeon rather than in the hands of men who deal occasionally with fractures. In that way the individual who handles fractures gets plenty of practice, and as Dr. Hammond of Easton, Md., pointed out in a paper read before this section two years ago, it accomplishes astounding results. I have been following his work for years and I want to say that that is one point wherein the medical profession by unselfish cooperation can accomplish a lot for its patients.

DR. DONALD E. MCKENNA, Brooklyn: Dr. Thomson has created a group of surgical commandments which are highly commendable. If each hospital or staff would arrive at such a formula as his institution has, it would be a great advantage in the management of compound fractures. Plenty of our large city hospitals do not see too many compound fractures. I had a hasty survey made yesterday of the Methodist Hospital fracture service. Of 1,264 fractures, there were only fifty-four compound fractures in the last two years and some odd months, or 4.2 per cent, whereas from a definite knowledge of a small suburban hospital within 100 miles of New York, I know that the incidence is over 10 per cent. Except in large industrial centers and in places among our urban population where compound fractures are liable to occur, on the waterfront, and elsewhere, even general hospitals do not see too many of these lesions. The compound fractures are emergency procedures. It is an error to temporize. The small puncture wound should be enlarged. To deny its potential wickedness is to abrogate the virtues of proper transportation, prophylactic tetanus and perfringens therapy, and efficient control of shock and proper immobilization. There is a school of thought which teaches that irrigation is to be avoided. I am in accord with the author who advocated mechanical flushing, not with a medicine dropper or bulb syringe but, to quote Dr. Thomson, "with a stream of flowing warm sterile water from an elevated jar, through a sterile tube." I would add the precaution about leaving bone fragments which are in any sense attached to viable tissue in situ. In débridement one is apt to sacrifice some of these fragments. When a compound lesion is close to a joint, I prefer skeletal traction rather than internal fixation, but when otherwise I am in accord with

The results of these investigations showed that destruction of the adrenal cortex was followed by a marked excretion of sodium and chloride in the urine, a pronounced drop in the blood concentration of these ions, an increase in the blood potassium, and hemoconcentration and nitrogen retention. Treatment was directed toward reestablishment of a normal blood electrolyte pattern. This was accomplished both with the aid of injections of cortical extract and with the addition of large quantities of salt (from 10 to 20 Gm.) to the diet. Wilder and his co-workers³ pointed out the importance and need for the restriction of the potassium intake in the diet.

Although this represented an improvement in the treatment of Addison's disease, it still left much to be desired. The adrenal cortex extract was available in limited quantities and was of limited potency. The large quantities of salt which patients had to consume were irksome to them, and the improvement in the general condition of these patients was not unduly striking. It was evident that further advancement in the treatment of this disease was dependent on the preparation of a more potent extract which could preferably be prepared synthetically.

In 1936 and 1937 Mason, Myers and Kendall⁴ and de Fremery and his co-workers⁵ isolated corticosterone and dehydrocorticosterone in crystalline form from the extracts of the adrenal cortex and found that they could maintain adrenalectomized animals in good condition. A short while later, Steiger and Reichstein⁶ announced the preparation of desoxycorticosterone acetate from stigmasterol, and subsequently Reichstein and von Euw⁷ succeeded in recovering this compound from an extract of the adrenal cortex. Levy-Simpson⁸ used desoxycorticosterone acetate in the treatment of two patients with Addison's disease and found that it exercised an effect qualitatively similar to that of adrenal cortex extract.

In 1938 Thorn and his co-workers⁹ used desoxycorticosterone acetate in the treatment of bilaterally adrenalectomized dogs. They found that it was effective in maintaining these animals in good condition despite a diet low in sodium and chloride. Withdrawal of the drug resulted in a prompt diuresis with loss of sodium and chloride ions in the urine, a decrease in urinary potassium, hemoconcentration and elevation of blood nonprotein nitrogen, and the development of symptoms of adrenal insufficiency. Thorn, Howard and Emerson¹⁰ subsequently used this compound in the treatment of eight patients with Addison's disease. They found that treatment in doses of from 2 to 30 mg. daily resulted in a marked improvement in the clinical con-

dition of the patient, as well as the restoration of the blood electrolyte pattern to normal. These changes occurred without supplementary treatment with sodium salts or a decrease in the potassium content of the diet. The authors felt that results of treatment with desoxycorticosterone acetate resembled in every way the effect obtained with a potent cortical extract. Ferrebee, Ragan, Atchley and Loeb¹¹ treated thirteen patients with Addison's disease with intramuscular desoxycorticosterone acetate and propionate. They found that improvement was greater than from any previous therapy. Their results were in general agreement with those reported by Thorn and his group.¹⁰ In three of their patients, however, definite hypertension developed during the course of treatment, and ten of their patients had edema, which varied from mild puffiness of the face and ankles to massive anasarca. Of this group of ten, cardiac insufficiency developed in three.

In 1937 Deanesly and Parkes¹² reported that the subcutaneous implantation of pellets of estrogens and androgens produced a prolongation of the hormonal effect. Ingle and Mason¹³ succeeded in prolonging the survival period of adrenalectomized rats by implanting subcutaneously tablets composed of a mixture of cholesterol and compounds derived from the adrenal cortex. Thorn and his co-workers,¹⁴ utilizing the technic employed by Deanesly and Parkes, studied the effect of subcutaneously implanted pellets of desoxycorticosterone acetate in bilaterally adrenalectomized dogs and six patients with Addison's disease. They find that results obtained with the pellets are similar to those with intramuscular injections except that the former effect a greater economy in the use of the drug. They conclude that the life of a pellet depends on its consistency and weight. The quantity of desoxycorticosterone acetate liberated appears to vary with the surface area of the pellet. The pellets are absorbed at the rate of 0.25 to 0.40 mg. daily.

RESULTS

In the present paper we present the results obtained in five patients with Addison's disease, who were treated with intramuscular injections of desoxycorticosterone acetate in oil. Four of these patients subsequently received pellets of the synthetic crystalline compound implanted subcutaneously. One of the patients was a female and four were males. Their ages varied between 11 and 44 years. All the patients had been previously treated with large amounts of salt by mouth, and four of them at some time or other received injections of adrenal cortex extract:

CASE 1.—D. G., a woman aged 21, was admitted to the hospital March 21, 1938, because of marked asthenia, pigmentation, nausea and loss of 20 pounds (9 Kg.) in weight. The blood pressure could not be determined by auscultation, but by palpation the systolic pressure was found to be 70. The blood urea nitrogen was 17 mg. per hundred cubic centimeters,

3. Wilder, R. M.; Snell, A. M.; Kepler, E. J.; Rynearson, E. H.; Adams, Mildred, and Kendall, E. C.: Control of Addison's Disease with a Diet Restricted in Potassium: A Clinical Study, *Proc. Staff Meet., Mayo Clin.* **11**: 273 (April 29) 1936.

4. Mason, H. L.; Myers, C. S., and Kendall, E. C.: Chemical Studies of the Suprarenal Cortex, *J. Biol. Chem.* **116**: 267 (Nov.) 1936.

5. de Fremery, P.; Laqueur, E.; Reichstein, T.; Spanhoff, R. W., and Uylert, I. E.: Corticosterone, a Crystallized Compound with the Biological Activity of the Adrenal-Cortical Hormone, *Nature, London* **139**: 26 (Jan. 2) 1937.

6. Steiger, Marguerite and Reichstein, T.: Desoxy-Corticosterone (21-Oxy-Progesterone aus Δ^3 -Oxy-ätiol Choleensäure), *Helvet. Chim. acta* **20**: 1164, 1937.

7. Reichstein, T., and von Euw, J.: Ueber Bestandteile der Nebennierenrinde: Isolierung der Substanzen Q (Desoxy-Corticosteron) und R sowie weiterer Stoffe, *Helvet. chim. acta* **21**: 1197, 1938.

8. Levy-Simpson, Samuel: The Use of Synthetic Desoxycorticosterone Acetate in Addison's Disease, *Lancet* **2**: 557 (Sept. 3) 1938.

9. Thorn, G. W.; Engel, L. L., and Eisenberg, Harry: The Effect of Corticosterone and Related Compounds on the Renal Excretion of Electrolytes, *J. Exper. Med.* **68**: 161 (Aug.) 1938; Studies on Desoxycorticosterone, a Synthetic Adrenal Cortical Hormone, *Endocrinology* **23**: 39 (July) 1939.

10. Thorn, G. W.; Howard, R. P., and Emerson, Kendall, Jr.: Treatment of Addison's Disease with Desoxycorticosterone Acetate, a Synthetic Adrenal Cortical Hormone, *J. Clin. Investigation* **18**: 449 (July) 1939.

11. Ferrebee, J. W.; Ragan, Charles; Atchley, D. W., and Loeb, R. F.: Desoxycorticosterone Esters: Certain Effects in the Treatment of Addison's Disease, *J. A. M. A.* **113**: 1725 (Nov. 4) 1939.

12. Deanesly, R., and Parkes, A. S.: Factors Influencing the Effectiveness of Administered Hormones, *Proc. Roy. Soc., London, S. B* **124**: 279 (Dec. 7) 1937; Further Experiments on the Administration of Hormones by the Subcutaneous Implantation of Tablets, *Lancet* **2**: 606 (Sept. 10) 1938.

13. Ingle, D. J., and Mason, A. L.: Subcutaneous Administration of Cortin Compounds in Solid Form to the Rat, *Proc. Soc. Exper. Biol. & Med.* **39**: 154 (Oct.) 1938.

14. Thorn, G. W.; Engel, L. L., and Eisenberg, H.: Treatment of Adrenal Insufficiency by Means of Subcutaneous Implants of Pellets of Desoxycorticosterone Acetate (a Synthetic Adrenal Cortical Hormone), *Bull. Johns Hopkins Hosp.* **64**: 155 (March) 1939. Thorn, G. W.; Howard, R. P.; Emerson, Kendall, Jr., and Firor, W. M.: Treatment of Addison's Disease with Pellets of Crystalline Adrenal Cortical Hormone Implanted Subcutaneously, *ibid.* **64**: 339 (May) 1939.

blood chlorides 93 milliequivalents per liter, sodium 131.3 milliequivalents per liter and sugar 79 mg. per hundred cubic centimeters. She was treated with a constant intravenous drip of isotonic saline solution and during the ensuing twenty-four hours received approximately 3,000 cc. As a result of the intravenous therapy she improved sufficiently to continue oral treatment with salt. During the course of the next week she was given 9 Gm. of sodium chloride and 4 Gm. of sodium bicarbonate daily by mouth. Her blood pressure rose to 95 systolic, 60 diastolic; the weight was 113 pounds (51 Kg.). The blood chemistry values had now altered, so that the sodium was 138.3, chlorides 100.0 and potassium 6.3 milliequivalents per liter. The blood sugar rose to 100 mg. per hundred cubic centimeters; the urea nitrogen, however, remained stationary at 16 mg. From June 16 to 19, approximately three months, after oral treatment with salt had been started, the patient without our knowledge omitted her daily supplementary

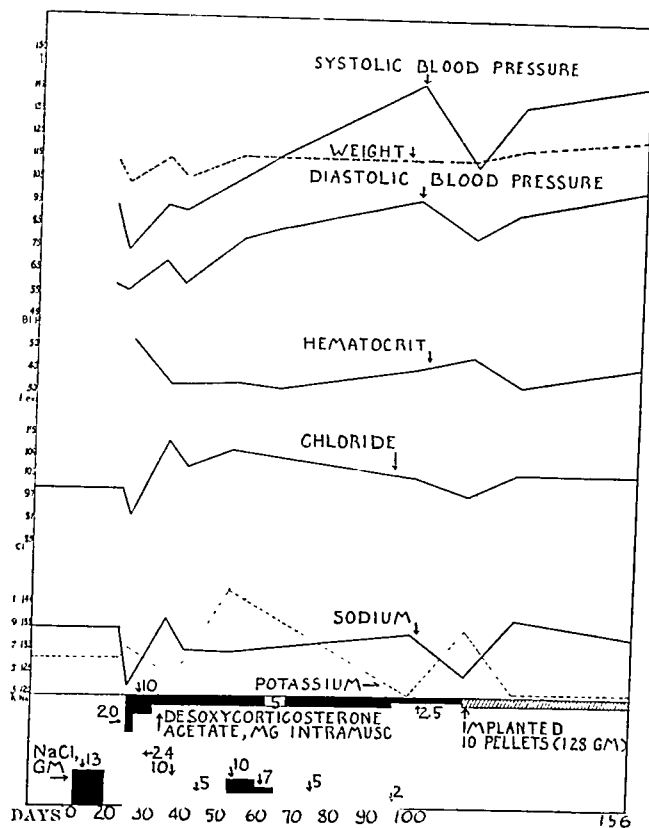


Chart 1.—Course in case 1.

salt feedings and was promptly precipitated into addisonian crisis. The blood pressure fell to 75 systolic, 58 diastolic. The blood values were sodium 122.3, chlorides 93.5 and potassium 7.2 milliequivalents per liter. The urea nitrogen was 34 and sugar 90 mg. per hundred cubic centimeters. The carbon dioxide content was 22.6 millimols per liter. The volume of packed red cells was 54 per cent, and the body weight had fallen to 104 pounds (47 Kg.).

During the three months period in which the patient was treated with salt alone, we find that the blood electrolytes were maintained at a fairly normal level. However, at no time did she feel well. She continued to complain of profound asthenia and anorexia and could spend but little time out of bed. June 19, when the symptoms of crisis developed, intramuscular injections of desoxycorticosterone acetate were started. She received 20 mg. of the synthetic substance daily for two days, then 10 mg. daily for four days. In addition, during this six day period she received 16 Gm. of salt by mouth daily. At the end of this period her weight had risen to 116 pounds (53 Kg.), the blood pressure was 90 systolic, 65 diastolic and the hematocrit reading had fallen to 35 per cent. The blood values now were sodium 139.9, chlorides 113.5 and potassium

5.1 milliequivalents per liter; the urea nitrogen was 12 mg. per hundred cubic centimeters and the carbon dioxide content was 23.0 millimols per liter. From June 24 until July 15 the patient received 10 Gm. of supplementary salt by mouth and 5 mg. of desoxycorticosterone acetate intramuscularly daily, but from July until the end of the first week in September the daily supplementary salt intake was reduced to 5 Gm. At the end of this period the patient's clinical condition improved remarkably. She was up and out of bed, she had a sense of well-being, her appetite had improved, and the pigmentation had decreased somewhat. The blood pressure was now 150 systolic, 94 diastolic; the weight was 117 pounds (53 Kg.). The blood electrolyte studies showed the sodium to be 137.8 milliequivalents per liter, urea nitrogen 10 mg. and sugar 90 mg. per hundred cubic centimeters, carbon dioxide 24.8 millimols per liter, and the blood hematocrit value 43 per cent. Because of the hypertension, the supplementary salt feedings were entirely discontinued, and the desoxycorticosterone acetate was reduced to 2.5 mg., given intramuscularly daily. After one week of this regimen the blood pressure fell to 112 systolic, 78 diastolic; the blood sodium was 127, chlorides 102 and potassium 9.2 milliequivalents per liter. It was obvious that 2.5 mg. of the drug given intramuscularly daily without additional salt was inadequate to maintain a normal electrolyte pattern. Despite the abnormalities of the blood constituents, however, her sense of well-being continued, and the patient was up and about without any discomfort.

September 16 ten pellets of crystalline desoxycorticosterone acetate were implanted subcutaneously, the average weight of each pellet being 128 mg. It was calculated that approximately 0.3 mg. of the compound would be absorbed daily per pellet, the total daily amount being 3 mg. This is equivalent in therapeutic effect to about 5 mg. given intramuscularly. She received no supplementary salt by mouth. One week after the implantation of the pellets her weight was 120 pounds (54 Kg.), the blood pressure was 138 systolic, 92 diastolic, and the hematocrit level had fallen to 34 per cent. The blood values now were sodium 141.8, chlorides 107.5 and potassium 3.6 milliequivalents per liter. She felt perfectly well and was discharged from the hospital. November 10, two months after implantation of the pellets, the blood pressure had risen to 150 systolic, 95 diastolic, and on slight exertion it would rise to 180 systolic, 110 diastolic, which was associated with dyspnea and cardiac palpitation. Her weight was 122 pounds (55 Kg.), and the blood electrolytes were entirely normal.

During the period of treatment with desoxycorticosterone acetate there occurred a tremendous improvement as far as the symptoms related to the Addison's disease were concerned, despite the fact that no additional salt was required. However, the symptoms of mild cardiac failure were a cause for considerable concern; they were probably due to the liberation of excessive amounts of the desoxycorticosterone acetate. She is to be readmitted to the hospital for the removal of some of the implanted pellets.

CASE 2.—S. R., a man aged 19, was admitted to the hospital Nov. 25, 1938, with all the characteristic signs and symptoms of Addison's disease. On admission, the hemoglobin was 101 per cent and the red blood cell count was 7,500,000, showing considerable hemoconcentration. The blood sodium was 128.3, chlorides 85 and potassium 8.1 milliequivalents per liter. The blood urea nitrogen was 27 mg. and the sugar 100 mg. per hundred cubic centimeters. His weight was 113 pounds (51 Kg.) and blood pressure 90 systolic, 50 diastolic. The patient was given 12 Gm. of sodium chloride and 4 Gm. of sodium bicarbonate daily by mouth. In addition, during the first two weeks he received 2 cc. of adrenal cortex extract subcutaneously daily. After seven weeks of treatment with salt alone he was discharged from the hospital considerably improved, although he continued to complain of weakness and some anorexia. His blood pressure on discharge had risen to 112 systolic, 70 diastolic, and the blood sodium had increased to 135 milliequivalents per liter.

He was readmitted to the hospital May 19, 1939. During the intervening six months period he had been taking daily 12 Gm. of salt and 4 Gm. of sodium bicarbonate. His weight had increased to 133 pounds (60 Kg.), and the blood pressure was 110 systolic, 80 diastolic. The blood chemical values now were sodium 133.1, chlorides 100 and potassium 9.6 milliequivalents per liter, urea nitrogen 15 and sugar 90 mg. per hundred cubic centimeters, and carbon dioxide content 25.5 millimols per liter. During this period of supplementary salt treatment he continued to feel weak, had one or two daily episodes of nausea and was entirely incapable of doing any work.

One week after his readmission to the hospital, treatment was begun with desoxycorticosterone acetate. He received a daily intramuscular injection of 5 mg. of the drug in oil, and the supplementary sodium chloride intake was reduced to 10 Gm. After one week of this treatment, the blood electrolytes returned to normal levels, the sodium increasing to 137.8 and chlorides to 105 milliequivalents per liter. His weight increased to 138 pounds (63 Kg.), but the blood pressure stayed relatively stationary at 105 systolic, 65 diastolic. Despite the improvement in blood chemistry values there occurred no change in symptoms. He continued to complain of weakness and occasional episodes of nausea. Three weeks after the intramuscular injections were started, ten pellets of crystalline desoxycorticosterone acetate were implanted subcutaneously in the right infrascapular region. The average weight of each pellet was 103 mg. For two days after the implantation of the pellets he continued to receive the supplementary 10 Gm. of salt by mouth. At the end of this period he began to complain of headache, vomiting, edema of the face and hands, palpitation and exertional dyspnea. It was noted that a gallop rhythm had developed. His weight at this time was 138 pounds and the blood pressure had risen to between 130 systolic, 85 diastolic, and 136 systolic, 102 diastolic. The blood electrolytes, however, showed no material change from the previous levels. The sodium was 137.7, chlorides 108.5, and potassium 7.1 milliequivalents per liter. The urea nitrogen was 10 and the sugar 80 mg. per hundred cubic centimeters, while the carbon dioxide content was 23.9 millimols per liter. The daily salt intake was promptly reduced and the headache, vomiting, and edema disappeared. On discharge from the hospital July 18, 1939, one month after implantation of the pellets, he was taking only 2 Gm. of additional salt by mouth, his weight was 139 pounds (63 Kg.) and the blood pressure 124 systolic, 80 diastolic. The blood electrolytes were entirely normal. Symptomatically there occurred a marked improvement. He felt quite strong and was anxious to return to work. Anorexia and nausea had entirely disappeared. He has been followed regularly with repeated blood chemistry determinations. In October 1939 the additional salt by mouth was entirely discontinued. In December 1939, six months after implantation of the pellets, the patient continues to feel extraordinarily well. His blood pressure, however, has risen to 140 systolic, 90 diastolic. The blood electrolyte pattern continues to remain normal.

This patient, like the one previously described, could get along only poorly when treated with large amounts of salt alone. Even after administration of a potent adrenal cortex extract there was but little change in the clinical condition, although the blood chemical constituents were approximately normal. Following the administration of the desoxycorticosterone acetate, however, there occurred marked improvement in symptoms, the most striking of which was the tremendous increase in the sense of well-being. There were improvement in strength and appetite and a complete disappearance of the gastrointestinal symptoms. However, on implantation of pellets there developed hypertension and edema and some signs of heart failure, although relatively mild in degree.

CASE 3.—J. S., a man aged 44, was admitted to the hospital May 24, 1939, because of pigmentation, progressive asthenia and fatigue, anorexia, nausea, and loss of 16 pounds (7 Kg.)

in weight in two weeks. His blood pressure on admission was 100 systolic, 75 diastolic and he weighed 118 pounds (53.5 Kg.). He presented a characteristic picture of Addison's disease in mild crisis. The blood chemical values were sodium 127.6 and chlorides 94.0 milliequivalents per liter, urea nitrogen 19 mg. and sugar 105 mg. per hundred cubic centimeters. Treatment was begun with 15 Gm. of salt by mouth daily in addition to the salt content of the usual ward diet. At the end of one month of this regimen, his weight was still 118 pounds and the blood pressure 105 systolic, 65 diastolic. The blood sodium rose only slightly to 130.5 and chlorides to 97 milliequivalents per liter while the potassium was 7.4 milliequivalents. The blood urea nitrogen was 14 mg., and the volume of packed red blood cells was 41.5 per cent. There was no improvement in the clinical condition. He continued to complain of profound weakness, anorexia and nausea. June 29, in addition to treatment with 15 Gm. of salt, intramuscular injection of 5 mg. of desoxycorticosterone acetate daily were started. After eleven days of the combined therapy his weight increased to 125 pounds (57 Kg.), the blood pressure rose to 125 systolic, 80 diastolic,

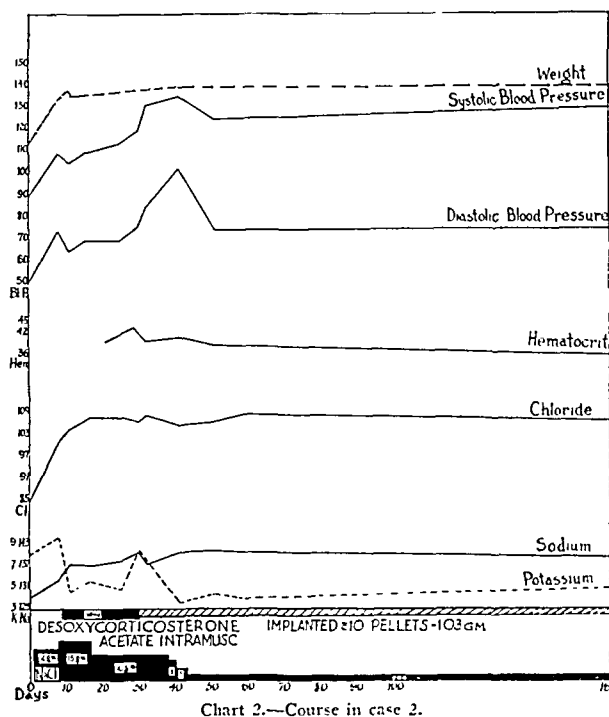


Chart 2.—Course in case 2.

and the hematocrit value dropped to 28 per cent. The blood electrolytes now were perfectly normal. The blood sodium was 138.3, chlorides 105.5 and potassium 4.5 milliequivalents per liter, while the urea nitrogen was 13 and the sugar 90 mg. per hundred cubic centimeters. The carbon dioxide content of the blood was 29 millimols per liter. Although there occurred this marked improvement in the laboratory observations, clinical improvement was not so striking. The anorexia and nausea had subsided considerably but the patient continued to complain of weakness. The supplementary sodium chloride intake was reduced to 10 Gm. daily, and seventeen days later thirteen pellets of the crystalline desoxycorticosterone acetate were implanted subcutaneously in the left infrascapular region. The average weight of each pellet was 126 mg. It was calculated that the daily absorption of the drug from the pellets would total 3.9 mg. Six weeks after implantation of the pellets the symptoms of Addison's disease had improved considerably. Anorexia and nausea had vanished, and the patient felt considerably stronger. However, he now began to complain of precordial pain on exertion, dyspnea and cardiac palpitation. The precordial pain was somewhat relieved by glyceryl trinitrate. The blood pressure at this time was 140 systolic, 85 diastolic, the hematocrit value was 33.5 per cent and blood

sodium 139, chlorides 105 and potassium 5.9 milliequivalents per liter. The supplementary salt by mouth was entirely discontinued but the precordial discomfort continued and the patient was now seriously handicapped by his cardiac symptoms. Two months after implantation of the pellets the blood electrolytes continued to be normal but the blood pressure varied from 150 systolic, 80 diastolic to 184 systolic, 98 diastolic. It was decided to remove some of the implanted pellets, and September 26 four pellets were removed surgically.

The blood pressure promptly fell to 140 systolic, 85 diastolic and the attacks of palpitation and precordial pain were somewhat less frequent. At present, one month after removal of the four pellets, the blood pressure continues at 145 systolic, 88 diastolic, his weight is 121 pounds (55 Kg.) and the blood sodium is 137.5, chlorides 102.5 and potassium 3.6 milliequivalents per liter. The blood urea nitrogen is 7.0 and the sugar is 80 mg. per hundred cubic centimeters. The patient has had no additional salt during this period. However, the anginal symptoms persist, although with somewhat lessened intensity.

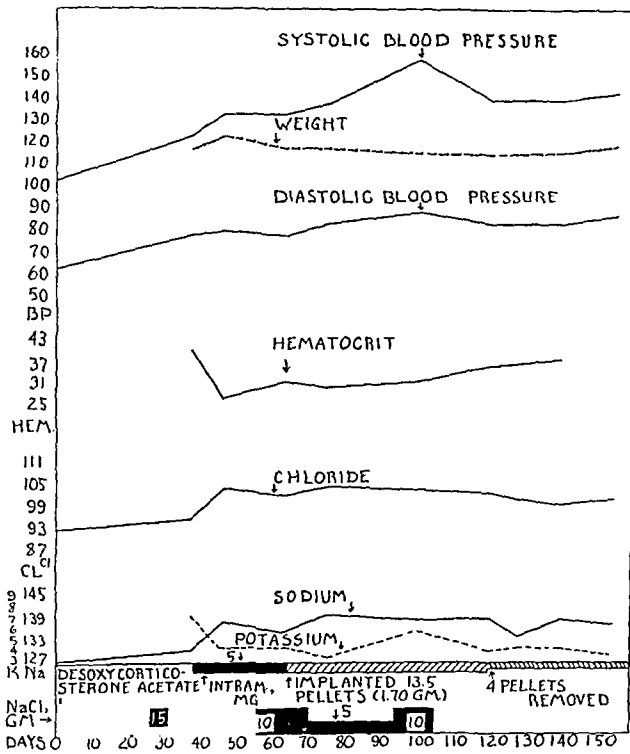


Chart 3.—Course in case 3.

We feel that it will be necessary to remove more pellets, despite the fact that the amount of the drug being absorbed is only approximately 2.7 mg. daily.

This patient represents the third of this series, all of whom have behaved in essentially the same fashion. After treatment with desoxycorticosterone acetate they progressed remarkably well from the point of view of Addison's disease. This subjective and objective improvement continued without the necessity for taking additional salt by mouth. However, in all three patients hypertension has developed, and in two of them it was severe enough to warrant removal of some of the implanted pellets.

CASE 4.—L. C., a man aged 34, was admitted to the hospital Nov. 20, 1939, after being treated elsewhere for Addison's disease. For a month prior to admission to the hospital he had received 16 Gm. of salt by mouth daily, plus injections of 5 cc. of adrenal cortex extract twice a week. On admission to the hospital his weight was 129 pounds (58.5 Kg.), blood pressure 94 systolic, 66 diastolic and hematocrit value 47 per cent. The blood sodium was 127 and chlorides 100 milli-

equivalents per liter. The blood urea nitrogen was 21 and sugar 95 mg. per hundred cubic centimeters. The carbon dioxide content was 26.5 millimols per liter. From November 20 until November 30 he was treated with 15 Gm. of salt by mouth without any additional extract. At the end of this period of time, he had lost 2 pounds (0.9 Kg.) in weight but there was no change in the blood electrolytes, blood pressure or hematocrit reading. He continued to complain of nausea and profound asthenia, and the intensity of pigmentation increased. November 30, daily intramuscular injections of 5 mg. of desoxycorticosterone were started in addition to the 15 Gm. of salt. There occurred an immediate improvement in clinical symptoms and by December 11 he felt well enough to get out of bed; nausea and anorexia had entirely disappeared and he felt considerably stronger. His weight at this time had increased to 132½ pounds (60 Kg.), blood pressure was 102 systolic, 68 diastolic and the hematocrit level had fallen to 39 per cent. The blood electrolyte pattern returned to normal, the blood sodium being 140.6 and chlorides 107 milliequivalents per liter; blood urea nitrogen was 6 mg. and sugar 60 mg. per hundred cubic centimeters, while the carbon dioxide content was 28.1 millimols per liter. December 19 the injected dose of desoxycorticosterone acetate was reduced to 2.5 mg. daily while the supplementary salt feeding had been decreased to 5.0 Gm. daily. Eight days later with this regimen his weight had increased to 136½ pounds (62 Kg.); the blood pressure and hematocrit level remained constant at 106 systolic, 64 diastolic and 38 per cent respectively. The blood sodium was 143.9 and chlorides 109 milliequivalents per liter, urea nitrogen 12 mg. and sugar 75 mg. per hundred cubic centimeters, and the carbon dioxide content was 25.8 millimols per liter. The desoxycorticosterone acetate was now reduced to 1.5 mg. with 5 Gm. of salt daily. Six days later there was no change in the weight or blood pressure, and the blood chemical constituents remained perfectly normal. Clinically the patient felt very well. Jan. 6, 1940, three pellets of crystalline desoxycorticosterone acetate were implanted subcutaneously in the left infrascapular region. The average weight of each pellet was 110 mg. and it was calculated that he would absorb approximately 0.9 mg. of the drug daily. In addition he receives 5 Gm. of salt by mouth. At present, two weeks after the implantation of the pellets, he continues to feel perfectly well and is anxious to go back to work. There has been no further change in his blood pressure, and the blood electrolytes remain normal.

In this case we attempted to avoid the development of the complications in other cases following the use of the synthetic compound. In previous cases the therapeutic goal desired was the ultimate treatment with desoxycorticosterone acetate without the supplementary daily salt feedings. This required the use of rather large amounts of desoxycorticosterone, and consequently there developed hypertension, edema or both. In this last case the amount of the substance decided on was less than the amount that would be required if no additional salt was to be used. To date this patient has had none of the sequelae seen in our patients treated with the large doses of desoxycorticosterone acetate. With the aid of a small amount of salt (5 Gm.) daily in addition to his regular diet he is doing extremely well.

CASE 5.—This case will be reported in greater detail elsewhere by the department of pediatrics of the hospital. Briefly, S. S., a boy aged 11, was admitted to the hospital April 15, 1938, in severe addisonian crisis, with a well defined history of Addison's disease of at least six months' duration. On admission his weight was 72 pounds (33 Kg.), blood pressure 64 systolic, 42 diastolic, blood urea nitrogen 51 mg. per hundred cubic centimeters, and blood sodium 114.7 and chlorides 85 milliequivalents per liter. He was given large quantities of intravenous saline solution and dextrose, and April 25 the blood pressure was still 66 systolic, 42 diastolic, blood urea nitrogen 26 mg. and sugar 100 mg. The blood electrolytes were sodium 120.5, chlorides 85 and potassium 6.9 milliequivalents per liter.

Clinically he was somewhat improved, although he continued to be listless and rather drowsy.

He was started on 10 Gm. of salt and 5 Gm. of sodium bicarbonate daily by mouth. Under this regimen he became more alert and seemed somewhat stronger. June 10, six weeks after oral salt therapy was begun, he was still seriously ill.

TABLE 1.—*Dextrose Tolerance Curves* in Patients with Addison's Disease Before and After Treatment with Desoxycorticosterone Acetate Blood Sugar, Mg./100 Cc.*

Patient and Type of Therapy	Control	$\frac{1}{2}$ Hour	1 Hour	2 Hours	3 Hours
1. D. K.					
Treatment with salt alone	55	85	125	110	95
Treatment with desoxycorticosterone acetate, 5 mg. intramuscularly for 68 days	75	125	105	90	85
2 months after pellets were implanted	70	135	115	120	120
2. S. R.					
Treatment with salt alone	85	90	85	85	70
Treatment with desoxycorticosterone acetate for 4 months (injections and pellets)	60	85	75	60	40
4. L. C.					
Treatment with salt alone	50	130	80	85	90
Treatment with desoxycorticosterone acetate for 3 weeks (injections)	90	105	100	85	80
5. S. S.					
Treatment with salt alone	60	115	80	90	90
Treatment with desoxycorticosterone acetate for 2 months (injections)	80	105	80	95	75

* 1.75 Gm. of dextrose per kilogram of body weight was administered to the fasting patient.

The blood urea nitrogen was 26 mg. and sugar 50 mg. per hundred cubic centimeters, while the blood sodium was 125.2 and chlorides 105 milliequivalents per liter, although the blood pressure had gone up to 96 systolic, 56 diastolic. At this point he began to receive 2 cc. of adrenal cortex extract subcutaneously in addition to the salt. Four months later (October 6) his weight had increased to 79 pounds (36 Kg.), the blood pressure was 100 systolic, 60 diastolic and the blood electrolytes were entirely normal. He was discharged from the hospital and during the course of the next year he received 15 Gm. of salt by mouth and 2 cc. of adrenal cortex extract subcutaneously twice a week. One year after discharge from the hospital, Oct. 4, 1939, he had gained 18 pounds (8 Kg.) in weight and felt fairly well; his blood pressure was 100 systolic, 70 diastolic, blood urea nitrogen 19 mg. and sugar 90 mg. per hundred cubic centimeters. The blood sodium was 139, chlorides 106.5 and potassium 3.6 milliequivalents per liter. The hematocrit value was 40 per cent. He was taken off salt and extract for about forty-eight hours; at the end of this period he began to complain of weakness, nausea and abdominal cramps. There was no change in blood pressure, but the hematocrit value increased to 43 per cent. The blood urea nitrogen had risen to 24 mg. The blood sodium had fallen to 135 and the chlorides to 101.5 milliequivalents per liter, while the potassium increased to 5.4 milliequivalents. October 10 treatment was begun with desoxycorticosterone acetate; during the course of the next month the daily dose was reduced to 1.5 mg., while he received 5 Gm. of additional salt by mouth. The patient felt well, the blood pressure was 104 systolic, 70 diastolic and the weight 99 pounds (45 Kg.), and the blood electrolytes were entirely normal. At this point it was decided to discontinue the desoxycorticosterone acetate entirely but to increase the daily supplementary salt intake again to 15 Gm. Two weeks later, although the blood chemistry values were still perfectly normal, he began to complain of some weakness and his appetite was reduced. His sense of well-being was not as marked as during the period of treatment with the desoxycorticosterone acetate.

COMMENT

The treatment of Addison's disease with desoxycorticosterone acetate represents a marked advance in therapy. It produces not only dramatic changes in the blood chemistry but equally striking changes in the well-being of the patient. The effect of the synthetic compound on the blood electrolytes is qualitatively the same as that with adrenal cortex extract except that the effect of the synthetic substance is more pronounced. With adequate doses of the desoxycorticosterone acetate there occur a retention of blood sodium and chloride and a potassium diuresis. With the reestablishment of a normal blood electrolyte pattern, evidences of dehydration and hemoconcentration disappear and the urea nitrogen returns to normal. In contrast to the effect of the synthetic drug on the blood electrolytes, no effect is produced on carbohydrate metabolism. In four cases (table 1) dextrose tolerance tests were done before and after treatment. There was no demonstrable change in carbohydrate metabolism as a result of the treatment. The tests were performed from three weeks to four months after therapy with the synthetic compound was started.

The effect of the desoxycorticosterone acetate on the blood pressure is apparently dependent on dosage. When the amount of the drug used is in excess of the daily requirement of the patient there will occur an increase in blood pressure which may even reach alarming levels. Thus three of our patients developed a definite hypertension, and one of this group manifested anginal symptoms which incapacitated him almost as completely as did the original uncontrolled Addison's disease. When the dosage is reduced the blood pressure will fall. Although the effect of the synthetic material on the blood pressure occurs promptly, hypertensive levels are not reached until after two to four weeks of constant therapy. It might be proper to point out here that treatment with the old adrenal cortex extract produced no marked changes in the blood pressure.

TABLE 2.—*Amount of Desoxycorticosterone Acetate Absorbed Daily from the Implanted Pellets as Determined by Removal of Pellets from Two to Six Months After Implantation*

Patient	Date of Implantation of Pellets	Weight of Pellets, Mg.	Date of Pellet Removal	Weight of Individual Pellets Removed, Mg.	Desoxy- corti- costerone Absorbed Daily, Mg.
1. D. G.	9/16/39	125	12/11/39	96.7	0.30
3. J. S.	7/27/39	126	9/25/39	110.9 110.9 114.9 110.0	0.28 0.28 0.20 0.20
			1/24/40	65.1 74.8 78.6 85.0	0.22 0.23 0.27 0.22

The effect of the synthetic drug on the pigmentation of Addison's disease is relatively slight and probably nonspecific in character. Following adequate treatment and after the general condition of the patient improved considerably there occurred some decrease in the intensity of the pigmentation. In no instance did the pigmentation entirely disappear. Whatever effect is exercised is probably the result of increased hydration of the patient.

The effect of the pellets is identical with that of the injection of the synthetic substance in oil. It must be

remembered, however, that when pellets are used the daily requirement of the desoxycorticosterone acetate is approximately from 60 to 75 per cent of that which is needed when the drug is given by injection. The pellets, then, have the advantage of being the more economical. However, after the pellets are implanted, control of the patient is difficult and the development of complications due to excessive medication requires surgical intervention to reduce the dosage. In deciding on the number of the pellets to be implanted in a patient with Addison's disease, the daily requirement must first be determined with intramuscular injections of the synthetic compound. Calculations are based on the fact that a pellet weighing from 100 to 150 mg. will liberate approximately 0.3 mg. of the drug daily (table 2). We feel that it is wiser to implant less than the required number of pellets and to supplement treatment with some additional salt by mouth (from 3 to 5 Gm.) daily. In this way the dangers of unfortunate complications are lessened. The dangers to be borne in mind in the use of this new drug are development of hypertension, edema and heart failure. The intelligent use of the synthetic compound requires careful clinical observation of the patient and adequate laboratory facilities for repeated blood electrolyte determinations. A word of caution must be said about indiscriminate use of this synthetic drug in various forms of asthenia. It is a powerful weapon, and until its pharmacologic actions are better understood its use should be restricted to patients with well defined Addison's disease.

SUMMARY

1. Five patients with Addison's disease were treated with intramuscular injections of desoxycorticosterone acetate in oil.

2. In four of these patients pellets of crystalline desoxycorticosterone acetate were subsequently implanted.

3. The disturbed blood electrolyte pattern is readily restored to normal with the aid of this new drug. It also exercises a marked salutary effect on the sense of well-being of the patients.

4. It produces marked increase in the blood pressure but exercises no effect on carbohydrate metabolism and on the pigmentation.

5. Pellets are more economical to use than are injections. They are, however, associated with greater danger of complications, since the control of the amount of the drug liberated is difficult and may require surgical intervention.

6. The dangers to be borne in mind with the use of the synthetic compound are development of hypertension, edema and heart failure.

7. Pellets weighing approximately 125 mg. liberate from 0.20 to 0.36 mg. of desoxycorticosterone acetate daily.

1155 Park Avenue.

Tuberculosis Death Rate.—In most parts of the world where statistics have been kept, the death rate from tuberculosis has been steadily declining for about one hundred years. About 1780 the estimated death rate from consumption in England was 650 per 100,000 living inhabitants. It is expected that the death rate in the United States will fall below 45 per 100,000 in 1940. According to Dublin, this will represent a decline of 37 per cent in the last ten years, and a decline of 61 per cent in the last twenty years. In forty years the death rate has dropped 76 per cent.—Webb, Gerald B.: Tuberculosis—Present and Future, *J. Lab. & Clin. Med.* 26:287 (Nov.) 1940.

ROENTGENOLOGIC GROUP EXAMINATIONS FOR PULMONARY TUBERCULOSIS

IN NEGROES IN CHICAGO: PRELIMINARY REPORT

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Because of the high incidence of tuberculosis among persons who have been exposed to massive infection from others, x-ray examinations of such contacts have been a routine practice in the Chest Clinic of the University of Chicago since 1929. The convincing experience that early tuberculosis is most successfully found among those who, because of the absence of symptoms, are unsuspected led in 1932 to the initiation of a case finding program among students, faculty and hospital employees. The results were in keeping with those

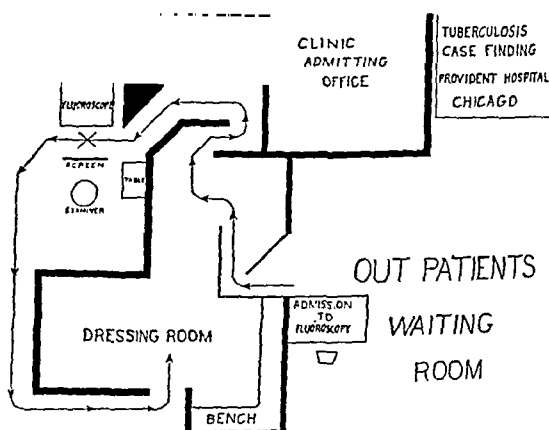


Fig. 1.—Arrows indicate route of patient through fluoroscopic plant.

reported from similar institutions and gratifying enough to continue the examinations as a university and hospital routine.

In 1934 the practice was extended to the expectant mothers seen in the clinic of the Chicago Lying-in Hospital because of the many unpleasant experiences with previously unrecognized tuberculosis among that group of patients and because they are an easily accessible group of healthy although physiologically strained persons. To date about 10,000 pregnant women have been examined. The published results from the first 4,000 indicated that slightly more clinically important tuberculosis is found by routine fluoroscopy of the chest than syphilis is by routine serologic tests.

SELECTION OF GROUP

Since the studies among the previously mentioned groups would not indicate the real proportions of the problem of unsuspected tuberculosis in the general population, it was desirable to gain access to still another

This work was financed by a grant from the Julius Rosenwald Fund. From the Department of Medicine, University of Chicago, and the Provident Hospital.

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group which, judged by its average economic status and according to published reports, would give a more accurate picture of the universal distribution of the disease. Because of our failure to reach those persons employed in the industries, we were glad to accept the generosity of the Julius Rosenwald Fund and the invitation of the Provident Hospital of Chicago to examine the patients in the outpatient department of that institution. The higher mortality of tuberculosis in the Negro than in the white population—in Chicago seven times higher—makes this a particularly suitable group. Furthermore, no large scale case finding program among Negroes carried out by x-ray examination has been reported from a metropolitan area until an extensive report was published by Edwards¹ from New York. His figures on the incidence of tuberculosis are close to our own. Of the proposed 30,000 examinations, 10,000 have been completed. The analyzed results and experience from the first 9,000 are presented in this preliminary report.

Although clinic patients cannot be considered a group of supposedly healthy persons, the application of the principle to examine all of them, regardless of the nature of their complaints, seems to have resulted in a fair cross section of the Negro population. To improve further the representative nature of the group, Negroes of nonpatient status were then invited to be examined. Up to the present time these nonclinical persons constitute nearly one third of the total number examined and tend to equalize the results of this survey with those of a wholly nonclinical group.

Although the object of the program is essentially the search for tuberculosis in adults, we included any children presented to us by relatives or guardians and, in addition, several special groups of juveniles (Boy Scouts and high school students). The distribution of nonclinic persons and clinic patients and the differential between new and return patients among the latter classification are indicated in table 5.

To avoid delay in the routine function of the clinic and to plan the program along with the work of the clinic staff, the examinations were carried out next to the waiting room of the outpatient department and admitting office. They precede the examinations in the clinics. A special fluoroscopic plant (fig. 1) was constructed through which large numbers of persons can pass in a very short time. A standard vertical fluoroscope was reconstructed to permit unhindered passage behind the screen (fig. 2). The examination of approximately 16,000 new patients annually together with return patients and special groups requires considerable speed and a minimum of friction in the organization.

The recording system consists of a form containing four different parts representing the diagnosis (to be attached to the clinic record), the results of examinations (which are retained by the investigators), a requisition blank for x-ray films and a memorandum for the social worker (fig. 3). The presence or absence of pathologic changes is indicated by checking the printed items. Very little writing is required. The patient's personal record is filled in by helpers who are provided by the WPA and NYA organizations.

CHARACTERISTICS OF GROUP

The 9,000 persons examined included 1,000 juveniles, consisting of two special groups examined: 506 members of Negro Boy Scout troops and 494 students of

one of the large Negro high schools of Chicago's south side. The average age for the entire group was 35.5 years, with a standard deviation of 15.5 years, which means that two thirds of the group fall between 20 and 51 years of age. These distributions are illustrated in figure 4.

Approximately twice as many females as males were examined, the proportion being 63.5 per cent females and 36.5 per cent males.

Approximately half of the total number examined were return patients to the Provident Hospital Clinic. The remainder were fairly evenly divided between new clinic patients and nonclinic persons.

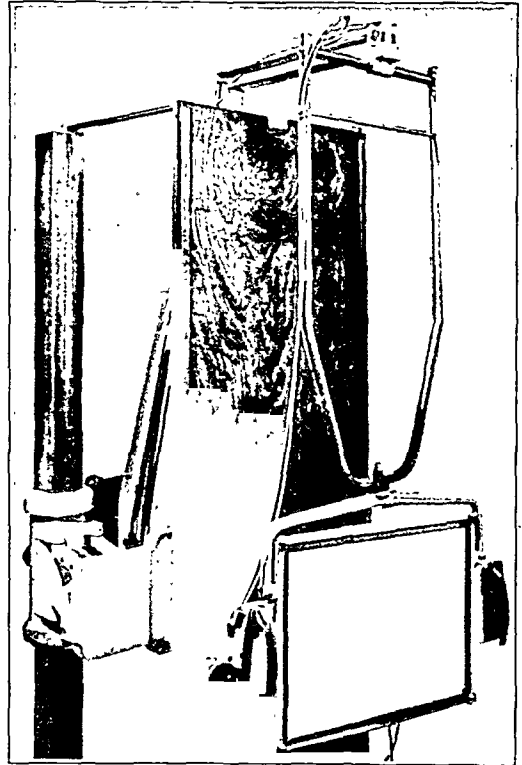


Fig. 2.—Vertical fluoroscope constructed for group examinations. Lateral arm has been replaced by overhead beam from which fluoroscopic screen is suspended, permitting continuous passage of patients behind screen from right to left. Shutter controls are attached to fluoroscopic screen by way of wire cables illustrated in the foreground.

Figure 5 shows the distribution for these three clinical classifications, for the entire group and without the 1,000 children.

OTHER OBSERVATIONS—NONPULMONARY DISEASE

In addition to finding disease in the lungs, it was inevitable that the fluoroscopic technic should reveal the presence of other, nonpulmonary, disease in the chest. In fact, 20 per cent of the total were found to have other disorders of the chest.

In most instances of the occurrence of nontuberculous disorders, x-ray examinations were not ordered. A complete analysis of the various nontuberculous conditions found has not yet been compiled. Very common were evidences of disease of the cardiovascular system, such as enlarged and mitral hearts, widened aortic shadows and aneurysms; evidence of old pleural involvement in the form of pleuritic residuals, some of them calcified. Scoliosis was not infrequent. One instance

1. Edwards, H. R.: Tuberculosis Case Finding: Studies in Mass Surveys. *Am. Rev. Tuberc. (supp.)* 41:3 (June) 1940.

of spontaneous pneumothorax (without symptoms) was discovered and a small number of cases of pneumonic infiltration, pulmonary tumor and other nontuberculous pulmonary diseases were found. Of the minor abnormalities of structure, various anomalies of the bony thoracic cage, including cervical ribs and vena azygos lobes, were the most common. Two cases of situs inversus were discovered. Among the 560 x-ray films taken, the most common nonpulmonary conditions were pleuritic residuals and cardiac enlargement.

ANALYSIS OF X-RAY FILMS

Among the 9,000 persons examined, in 574 instances (6.4 per cent) there were fluoroscopic changes sufficient to justify ordering x-ray examinations, one to every 15.7 persons examined. Of the 574 x-ray examinations ordered, 560 actually were done, or 97.6 per cent. Considering the difficulty of persuading persons to return a second time for the purpose of having the x-ray examination made, this figure is very high, and much

type of pathologic condition and as to the stage of the tuberculous disease.

Seventy-two per cent were minimal, 19 per cent moderately advanced and 9 per cent far advanced.

The productive-fibroid type of pathologic change was found to have the greatest incidence, occurring in 31.3 per cent of the cases. Second most frequent were the fibrocaceous and fibrocalciocaceous types, occurring in 22.5 per cent. The clinically important pathologic types, exudative caseous and exudative, occurred in 13.6 per cent and 9.9 per cent, respectively (table 2).

INCIDENCE OF DISEASE

To the 380 cases presenting positive signs on x-ray examination were added five cases in which the fluoroscopic observations were sufficiently definite to be unmistakable, making a total of 385 persons of the 9,000 examined, or 4.3 per cent, who were found to have definite pulmonary tuberculosis. Eighty-seven were judged to have clinically unimportant pulmonary disease

[illegible]

Fig. 3.—Type of record filled out for each patient examined by fluoroscopy. Sheets are numbered serially. Stub at left (A) is used only when important clinical disease is found, for purposes of clinical and social follow-up. Main portion of sheet (B), containing diagrammatic representation of pathologic condition, is attached to patient's clinic record. Upper right hand sheet (C) is retained in files permanently. It includes the final diagnosis made from x-ray films and the statistics for a study on tuberculous calcifications. Stub in lower right hand corner (D) is used only when x-ray examination is required and ordered on main portion of sheet (B) to confirm fluoroscopic examination.

of the success obtained in this regard was due to the unceasing efforts of the social service worker.

Of the fourteen persons who had manifestations on fluoroscopy not confirmed by x-ray examination (2.4 per cent of x-ray examinations ordered), five presented sufficiently definite conditions to be included with those judged to have tuberculosis. The other nine have been assumed to have no pulmonary disease or have clinically unimportant disease.

Of the 560 x-ray films taken, 32.2 per cent proved to show no pulmonary disease, 15.5 per cent to show definite but clinically unimportant pulmonary disease and 52.3 per cent showed definite pulmonary tuberculous pathologic changes judged to be of actual or potential clinical importance. Thus, in 380 instances x-ray films were positive, 77.1 per cent judged to be clinically important and 22.9 per cent clinically unimportant. These figures are summarized in table 1.

The 374 persons whose x-ray films were judged to show definite pulmonary changes were classified as to

(though in many instances such persons are under clinical observation and their contacts have been examined), an incidence of 1 per cent. Thus 298 persons, or 3.3 per cent of the entire group, proved to have clinically important pulmonary disease.

The incidence of tuberculosis was actually slightly greater than these figures indicate when the special groups of Boy Scouts and high school students were excluded, the respective figures for all pulmonary disease and clinically important tuberculosis then being 4.65 and 3.6 per cent (table 3).

INCIDENCE OF TUBERCULOSIS ACCORDING TO AGE

In conformity with the observations of many investigators, there was found to be a considerable difference in the incidence of tuberculosis in various age groups. In general, the incidence was above the average for the entire group below 10 years of age and above 45 and below the average for the group between the

ages of 10 and 45. Table 4 gives the figures for all positive pulmonary manifestations by age groups, for both the 1,000 children of the special groups and the 8,000 others examined.

TABLE 1.—*Clinical Classification of Cases Examined by X-Rays*

	Number	Per Cent	Per Cent All X-Rays
Pulmonary disease			
Clinically important.....	293	77.1	52.3
Not clinically important.....	87	22.9	15.5
Total pulmonary disease.....	380	100.0	
Negative.....	180		32.2
Total x-rays.....	560		100.0

TABLE 2.—*Classification of Cases of Tuberculosis Found by X-Ray Examination*

	Minimal	Moderately Advanced	Far Advanced	Total	Per Cent of Total
Exudative (predominantly exudative)	28	7	2	37	9.9
Exudative caseous.....	17	19	15	51	13.6
Caseous.....	4	0	1	5	1.3
Productive (fibroid).....	102	14	1	117	31.3
Fibrocasseous (fibrocalcicaseous).....	46	26	12	84	22.5
Calcicaseous.....	57	4	0	61	16.3
Calcified.....	15	1	0	16	4.3
Miliary, active.....	0	0	1	1	0.3
Miliary, healed, calcified.....	0	2	0	2	0.5
Totals.....	269	73	32	374	
Per cent total.....	71.9	19.5	8.6		100.0
Number with cavities.....	0	17	26	43	
Per cent cavernous.....	0.0	23.3	81.3		11.5

When only clinically important tuberculosis of the lungs is considered, there is also a marked variation as to the incidence in different age groups. The greatest incidence is in the very young and the old. As compared with a total group average incidence of 3.3 per cent, children under 15 and men and women above 50 were found to have a relatively high incidence and those between 15 and 50 a relatively low incidence. This is illustrated graphically in figure 6 for the group exclusive of the 1,000 juveniles. It is to be observed from these figures that persons in the third decade of life had the lowest incidence of important pulmonary disease.

INFLUENCE OF VARIOUS FACTORS ON INCIDENCE OF DISEASE

When the total group of 9,000 is subdivided into several categories, according to various criteria, and the incidence of tuberculosis in each category is calculated, additional information is gained as to where tuberculosis may be found. Table 5 summarizes these figures. The 1,000 Boy Scouts and high school students have been excluded from this analysis, and only clinically important pulmonary disease is considered, but inclusion of the 1,000 juveniles and of clinically unimportant pulmonary disease does not greatly alter the results.

Sex.—The incidence of clinically important pulmonary disease is approximately twice as frequent in males as in females.

Clinical Status.—Patients coming to the clinic for the first time have nearly half again as much tuberculosis as do patients previously registered and examined.

Nonclinic persons examined were found to have an incidence of clinically important pulmonary disease slightly higher than return clinic patients but definitely lower than new clinic patients.

Calcifications.—Those patients found to have calcifications, either parenchymal or glandular, proved to have more clinically important pulmonary disease than persons without such calcifications. This difference was more marked when the 1,000 children of the special groups were included.

COMMENT

In previous communications we have expressed and reiterated our trust in the fluoroscopic method of examination if it can be supplemented by chest films for all positive and suspected conditions. No detailed discussions of the merits of fluoroscopy as compared to other methods of x-ray examination are offered in this paper. An appraisal of the value of the various techniques employed in group examinations of the chest, including the tuberculin test, has been attempted in another article.^{1a} Recent controversy, however, induces

TABLE 3.—*Incidence of Positive Examinations*

	Number Examined	Clinically Unimportant	Clinically Important	Total Pulmonary Disease
		No. %	No. %	No. %
Special groups of children.....	1,000	5 0.5	8 0.8	13 1.3
Others.....	8,000	82 1.0	290 3.6	372 4.65
Totals.....	9,000	87 1.0	298 3.3	385 4.3

TABLE 4.—*Age Incidence of Positive Examinations, Clinically Important and Unimportant, in 1,000 Juveniles and 8,000 Others*

	Positive (Clinically Important and Unimportant)									
	Total Examined		Negative						Total Positive	
					Juveniles		Other			
	Juve- niles	Other	Juve- niles	Other	No.	%	No.	%	No.	%
0-4	0	30	0	28	0	0.0	2	6.7	2	6.7
5-9	37	140	37	134	0	0.0	6	4.3	6	3.4
10-14	490	232	484	241	6	1.2	11	4.4	17	2.3
15-19	468	517	461	499	7	1.5	18	3.6	25	2.6
20-24	5	706	5	685	0	0.0	21	3.1	21	3.0
25-29	0	899	0	866	0	0.0	33	3.7	33	3.7
30-34	0	994	0	956	0	0.0	38	3.8	38	3.8
35-39	0	1,077	0	1,029	0	0.0	48	4.5	48	4.5
40-44	0	909	0	863	0	0.0	46	5.1	46	5.1
45-49	0	718	0	689	0	0.0	29	4.0	29	4.0
50-54	0	618	0	578	0	0.0	40	6.5	40	6.5
55-59	0	485	0	446	0	0.0	39	8.0	39	8.0
60-64	0	334	0	313	0	0.0	21	6.3	21	6.3
65-69	0	178	0	169	0	0.0	9	5.1	9	5.1
70-74	0	45	0	36	0	0.0	9	20.0	9	20.0
75-79	0	10	0	8	0	0.0	2	20.0	2	20.0
80-84	0	2	0	2	0	0.0	0	0.0	0	0.0
85-89	0	1	0	1	0	0.0	0	0.0	0	0.0
Records missing	0	85	0	85	0	0.0	0	0.0	0	0.0
Total	1,000	8,000	987	7,628	13	1.3	372	4.65	385	4.3

us to add here that we consider fluoroscopy a wholly reliable method if it is employed by physicians who are well trained in pulmonary pathology and in the technic of the method. Its use is limited not by an inferiority to other means of examination in recognizing disease but rather by its inability to furnish an objective, per-

1a. Bloch, R. G.: Case Finding in Tuberculosis, to be published in the American Review of Tuberculosis, February 1941.

manent record of negative observations; this makes it impracticable wherever a liability for the examining agency may be involved as, for example, in the entrance examinations for the fighting forces. Employing fluoroscopy in the present survey but using single paper

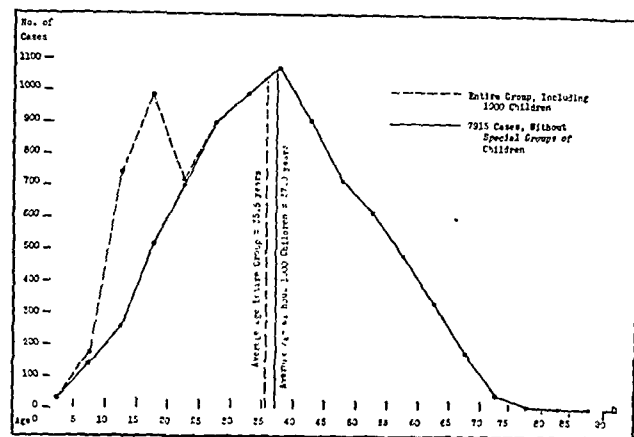


Fig. 4.—Age distribution of 8,915 persons examined by fluoroscopy.

roentgenograms for reasons of economy, we found that the paper films were not nearly as satisfactory for qualitative analysis of tuberculous lesions as is possible from transparent films. In the clinical appraisal of our observations we have refrained from using the terms "active" and "inactive" and similar qualifying adjectives. While the activity of many tuberculous lesions from x-ray diagnosis alone cannot be doubted, there are many in which only clinical and sometimes prolonged observation can decide the degree of activity. Certainly the absence of activity cannot be determined except perhaps in small and definitely calcified foci. The terms "clinically important" or "clinically unimportant" under which the results have been grouped are not meant to express final judgment as to the clinical importance of the lesion but only to give our impression gained from the chest films. As a rule, we are not in a position to follow most of the patients clinically. The great majority are referred to the health authorities for further observation and care. As yet too little time has elapsed to appraise the correctness of our impressions. We are

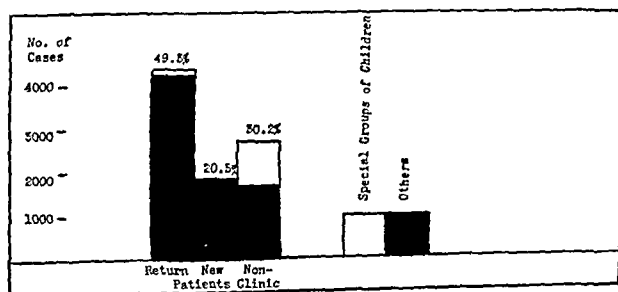


Fig. 5.—Clinical status of 8,915 persons examined by fluoroscopy.

aware of the large number of small tuberculous infiltrations to which we attach clinical significance. We know that this may evoke some criticism and occasional ridicule. There seems to be widespread and considerable discrepancy between the desire to make a diagnosis of early tuberculosis and the attention which it receives after it has been found. The circumscribed "spot in the lung," often presented as negligible to the patient and

remaining untreated, is one of the most frequent small forms of caseous tuberculosis which may excavate rapidly. In figure 7 is demonstrated the excavation of two such lesions, discovered in supposedly healthy persons during group surveys.

Figure 8 demonstrates how a similar small focus developed into advanced tuberculosis during a period of seven years. These roentgenograms are of patients of the white race. There is reason to assume that the same lesions in a Negro would have developed more rapidly, other factors being equal.

The greater tendency toward exudative tuberculosis and unfavorable progression of tuberculous disease in the Negro compared with observations in the white race seems well established and is attributed to a lesser immunity of the race.² There is no discrepancy between this experience reported from autopsies and the clinical predominance of the productive types of disease found in surveys. The average age of our adult group was 37 years, whereas the largest number of deaths from tuberculosis in Negroes occurs during the third decade in life. It seems, therefore, that a large proportion of

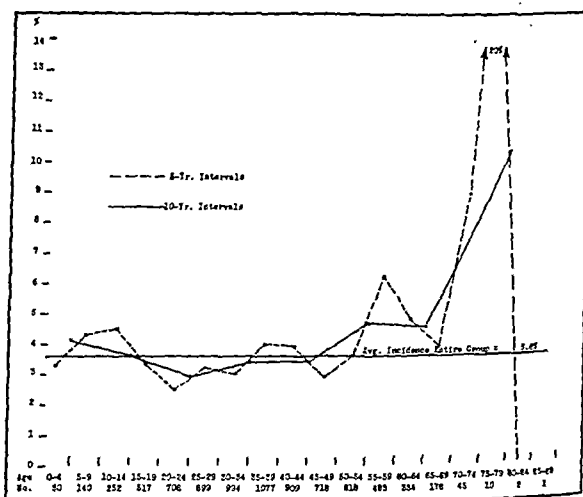


Fig. 6.—Incidence of clinically important pulmonary disease found on fluoroscopy, by five year and ten year age groups (8,000 cases).

our patients are those who have been able to survive early exudative lesions by favorable tissue response in the lung. However, many of them remain, at best, stationary without signs of definite healing, which explains the much higher incidence of clinically important lesions (3.3 per cent) among the total of pathologic changes (4.3 per cent) than have been found in the white population, in which the respective figures are 1.2 per cent and 3.5 per cent.

The striking preponderance of minimal over moderately and far advanced tuberculosis in our group is almost the reverse of the distribution found in sanatoriums³ (fig. 9). While it demonstrates the essential

2. Pinner, Max, and Kasper, J. A.: Pathological Peculiarities of Tuberculosis in the American Negro, *Am. Rev. Tuberc.* 26: 463-491 (Nov.) 1932. Israel, H. L., and Payne, H. M.: Tuberculosis in the Negro: Clinical and Roentgenological Characteristics, *ibid.* 41: 188-209 (Feb.) 1940.

3. Myers, J. A.: Collapse Therapy and the Ambulatory Patient, *J. Thoracic Surg.* 3: 175 (Dec.) 1933. Wherrett, G. J.: Follow-Up Information on 2,031 Tuberculosis Patients One to Thirteen Years After Discharge from Sanatoria, *Am. Rev. Tuberc.* 21: 62-73 (Jan.) 1935. Harper, F. R.: Phrenic Interruption Combined with Artificial Pneumothorax for Pulmonary Tuberculosis, *ibid.* 35: 475-483 (April) 1937. Franklin, R. M.; Zavod, W. A., and Perez, H. E.: The Frequency of Artificial Pneumothorax Refills in Tuberculosis: Preliminary Report, *ibid.* 35: 513-529 (April) 1937.

value of examinations among the unsuspected population, it may be due partly to the more frequent occurrence of productive lesions after the third decade of life and, to some extent, to our inability to bring under observation the patients with far advanced disease who

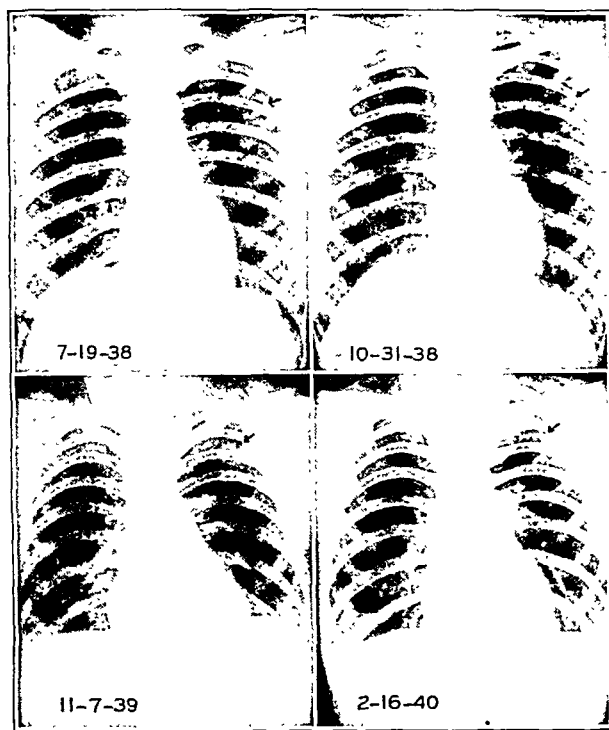


Fig. 7.—On the left, two patients with a subapical caseous minimal tuberculosis. On the right, the same lesions after excavation with resulting positive sputum and symptoms. The time interval during which excavation occurred in each case was about three months.

had been the source of infection of many of our patients with minimal infection. Insufficient funds did not permit the establishment of the extensive social service which would have been needed for that purpose. However,

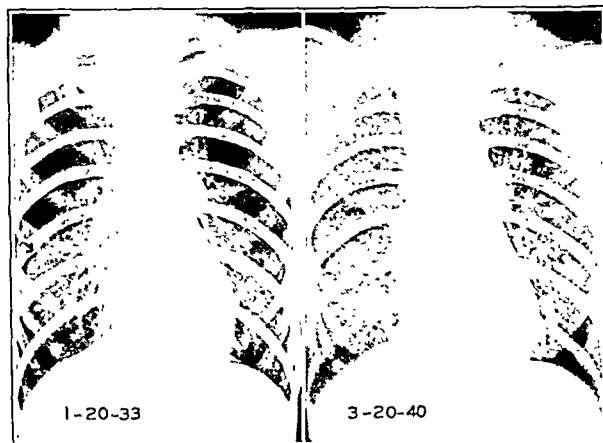


Fig. 8.—Small tuberculous focus seen at left proved to be of great clinical importance by subsequent development into far advanced tuberculosis, as demonstrated at right.

these persons do not remain unnoticed but are brought to the attention of the city health authorities.

The higher incidence in juveniles, which is recorded in table 4 as above the average incidence of the total group, is not in accordance with the general experience

concerning the age distribution of tuberculosis. Our higher figures seem to be due to a practice of considering any not definitely calcified lesion in children as clinically important in order to insure continued clinical observation.

The occurrence and significance of calcification is an object of special investigation of our study. The detailed results will be reported elsewhere. For epidemiologic considerations it is interesting to note that the incidence of clinical tuberculosis in the presence of calcification was 1.6 per cent greater, or half again as high as in persons without calcified foci. This observation again throws doubt on the traditional conception of the protective value of first tuberculous infections.

That a special search for tuberculosis in a general clinic is not superfluous is demonstrated by the incidence of 2 per cent clinical pulmonary disease in the return patients of the clinic. It is a common experience

TABLE 5.—Influence of Various Factors on Incidence of Clinically Important Pulmonary Disease (7,915 Cases, Exclusive of Special Groups of Children)

Category	Total Examined		Incidence	
	Number	Per Cent	Number	Per Cent
I. Sex				
Male.....	2,593	32.8	147	5.7
Female.....	5,322	67.2	143	2.7
Total.....	7,915	100.0	290	3.7
II. Clinical status				
Return patients.....	4,365	55.1	143	3.3
New patients.....	1,828	23.1	84	4.6
Nonclinic persons.....	1,722	21.8	63	3.7
Total.....	7,915	100.0	290	3.7
III. Calcifications				
With calcifications.....	1,426	18.0	72	5.0
Without calcifications....	6,489	81.1	218	3.4
Total.....	7,915	100.0	290	3.7

that pulmonary lesions are overlooked in examinations in specialized clinic departments largely because of insufficient use of x-ray diagnosis. However, not only pulmonary disease is revealed by the addition of this routine to clinic work; the examiner at the fluoroscope is in a position to call the clinician's attention to large numbers of patients with extrapulmonary disease. This is indicated by the incidence of 20 per cent of such extrapulmonary pathologic changes among which cardiovascular disease is the most prevalent. To a large measure the figure is due to the frequency of vascular syphilitic involvement but more significantly also to the occurrence of enlarged and otherwise abnormal cardiac shadows seen in children whom we were able to refer to clinical examination. This experience alone seems to justify fluoroscopic group examinations among children.

Altogether, our experience so far has justified the time, effort and expense⁴ required by the experiment;

4. The cost of the survey, estimated on the basis of an expected number of 30,000 examinations, will be 10 cents per examination and approximately \$3 for the discovery of each clinically important case of tuberculosis. Since all physicians participating in the examinations are donating their services, the available funds were used for the establishment of the plant, for the purchase of equipment and for administrative expenses. Adequate remuneration of the medical examiners would about double the cost per case. This would still be lower than the expenditure for other tuberculosis surveys concerning which the information was available.

we wish to emphasize the necessity of roentgenologic group examination in the fight against tuberculosis in Negroes as well as in other groups of the population. A clinic offers the opportunity to conduct a routine roentgenologic search for unsuspected tuberculosis in a never ending flow of the populace without the necessity of solicitation. Since dozens of cases of tuberculosis are missed throughout the country every year in physicians' offices, in clinics and in hospitals, since thousands go through life unconscious of their disease and therefore do not seek medical help, in other words since tuberculosis is still one of the most urgent problems in the preservation of the health of the people and, furthermore, since all this is due to two factors, namely (1) that physical examinations frequently fail to reveal the disease and (2) that much active tuberculosis causes no symptoms, it is the demand of our time and of the better knowledge acquired in recent years that all physicians, wherever they practice their profession and whatever their special medical interest may be, help to educate the people that tuberculosis must be searched for everywhere and in everybody.

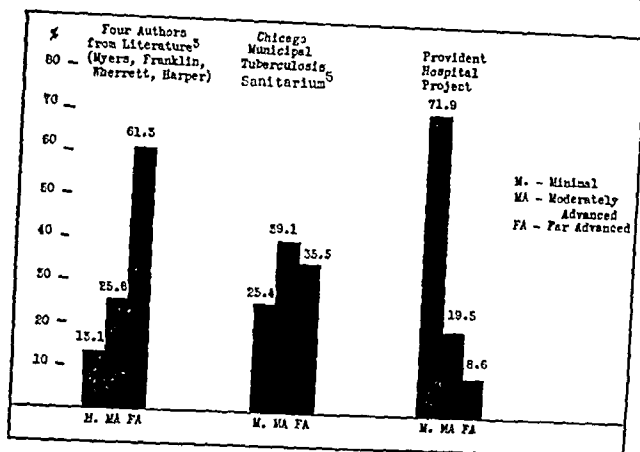


Fig. 9.—Comparison of stages of tuberculosis of groups under treatment in sanatoriums, reported to health authorities and found by fluoroscopy case finding program.

There is hope that group surveys on an ever increasing scale will be organized throughout the country and that we are not far from the day when laws and regulations will make an x-ray examination of the chest a prerequisite for employment in domestic service, in the teaching professions, in industry, in the fighting forces and for the issuance of a marriage license. It appears that there is a weapon available for the fight against tuberculosis which, without any spectacular advance in scientific research, can carry the profession far toward the elimination of the disease as a major public health menace.

The better opportunity of finding or, at least, of suspecting the presence of extrapulmonary disease adds to the value of such examinations in the admitting department of a general clinic. We suggest, therefore, that roentgenologic examination of the chest of all patients should become a routine procedure in all medical institutions.

950 East Fifty-Ninth Street.

ABSTRACT OF DISCUSSION

DR. MAX PINNER, New York: The authors have chosen the x-ray approach without previous tuberculin test. One should not draw general conclusions from this. Each worker should determine the feasibility or the advisability of doing tuberculin tests or not doing tuberculin tests before x-ray examination. In the population that Dr. Bloch and his collaborators have examined the incidence of negative reactors is undoubtedly minimal, and no saving would be had by doing tuberculin tests. On the other side, in rural communities it is probably advisable to do tuberculin testing first because from 50 to 70 per cent of x-ray films may be saved by this method. There is a great deal of discussion about the value and reliability of fluoroscopy as against roentgenography. I believe that it cannot be solved in a general way. Fluoroscopy presupposes, more than roentgenography, very careful training and experience, and whoever has it can probably go far with this method, complemented by x-ray films as indicated. In the surveys on Negroes, many were probably astonished that not a greater percentage was found; as a matter of fact, in surveys of Negroes and white people living under identical living conditions, such as done by Dr. Edwards in Harlem, the percentage of morbidity of Negroes was less than in white persons; nevertheless the mortality rate is a multiple of the white rate, indicating that the disease in Negroes is much shorter and much more rapid in development. This would indicate that an occasional survey in Negro groups is not of much use because not all the early cases which will develop next year are found in the surveys this year; it will be necessary to make the examinations at rather short intervals. The acuity of the disease in the Negro as compared with the white person I think is well exemplified by the autopsies such as my associates and I reported for Detroit and Chicago. One of the outstanding factors of differences statistically seen is the much greater frequency of disseminated lesions in the Negro as compared to the white person. Incidentally, in this autopsy work we were struck by the relative frequency of apparently completely healed, calcified, primary complexes in Negroes and particularly in Negroes who, on reinfection, developed lesions that looked very much like primary infections again. We concluded from that that the Negro who goes through his primary infection becomes allergic without increasing his immunity, as the white person apparently does.

DR. H. R. EDWARDS, New York: This paper in many instances is a close duplicate of the work we have been doing in New York. I should like to offer for comparison the results of 70,000 examinations in Harlem, by the rapid paper x-ray method, which I believe to be superior to fluoroscopy. The observations indicate in general about twice as much tuberculosis among the white population above 25 years of age as among the Negroes, whereas below that age the ratio is the reverse. In another study involving 53,000 recipients of home relief the same distribution by color and age was found. Our definition of clinically significant tuberculosis is essentially the same as that used by Dr. Bloch. The distribution by sex and color indicates white males 5.7 per cent, Negro males 3.4, white females 3.3, as compared with Negro females 2.2, an average of 3.1 considered active and 17 per cent considered arrested; also there is a higher percentage of arrested chronic pulmonary tuberculosis among white males and females than among Negro males and females. A chart representing some 169,000 individuals, ranging from high schools with four cases in a thousand to transient males with 43 cases per thousand convinces me that the problem of tuberculosis is closely allied to specific age, sex, racial and economic factors. It is primarily an adult problem, more serious among the Negroes and those living on low income or in tenement houses, and the unemployed than the employed and higher economic levels of society. About 70 per cent of the patients were found by the survey method in the minimal stage at a time before they have spread their infection to others and when the most can be done to restore them at the least cost to the community.

5. Tice, Frederick, and Hruby, A. J.: Collapse Therapy at the Chicago Municipal Tuberculosis Sanitarium: A Critical Study of 8,083 Cases, *Bull. City of Chicago Municipal Tuberc. Sanitar.* 15-16-17: 30, 1935-1936-1937.

DR. ARTHUR B. ROBINS, New York: I want to amplify some of the remarks made by Dr. Edwards in emphasizing the age factor in connection with the difference between white and Negro tuberculosis. I have been interested in the question of the relationship between mortality and morbidity. When I started this work I was struck by the fact that the group with the predominant mortality seemed to have the lower morbidity, and in every study that my associates and I have done that has been a consistent finding. Even in those under 25, among whom the morbidity in the Negro is higher in a ratio of about 4 to 1, the ratio of deaths is from 8 to 12 to 1; and, in those over 25 among whom the mortality is from four to five times as high, the morbidity is lower than in the white population. We have also been interested in the results of annual re-x-ray examinations of the patients and we have a group of about 9,000 individuals who were given x-ray examinations in the relief study in Harlem one year, and the negative ones given re-x-ray examinations the following year. In that group, which is made up of about 7,500 Negroes and 750 white persons, twenty-six cases of tuberculosis developed in people whose previous x-ray examinations had been entirely negative. It is of interest that twenty-one of those cases developed in the Negro group, two in the white group and three among Puerto Ricans. The incidence rates in those groups are approximately the same, although the group of 750 white individuals is too small to draw conclusions from. However, in an average period of eight months from the time of diagnosis, seven of the twenty-one cases developing in the Negroes have already proved fatal, indicating an annual mortality rate of 50 per cent in Negroes with negative x-ray examinations at the beginning of the study, who later developed tuberculosis. I think that this may have a great deal to do with the difference in morbidity and mortality figures, and I think it is rather an effective disposal of the objection that a major portion of those differences is related to the unwillingness of Negro patients to come in for x-ray examination or to accept treatment. We had no difficulty in getting those people, although they were classified as apparently healthy, back on two separate occasions, an average of a year apart.

DR. HAVEN EMERSON, New York: If Dr. A. J. Chesley of Minnesota is not in the room to give the information himself, I should like to call attention to a method of tuberculosis case finding that was applied, as far as I know, the first time in the laboratory of the Minnesota State Department of Health in the process of typing pneumonia sputum. All such pneumonia specimens were put through a routine examination for the tubercle bacillus, and 9 per cent were positive for the tubercle bacillus; of the cases of tuberculous infection so discovered, only 10 per cent had been previously reported as cases of tuberculosis to the state department of health. It is inexpensive, costing about 15 cents to have each pneumonia sputum examined for tubercle bacilli, and we are, as sanitarians, more concerned with the discovery of a case of tuberculosis with positive sputum in which recovery recently occurred from an acute pulmonary disease than with a large number of persons with relatively unimportant lesions, even though clinically significant, with negative sputum.

DR. ROBERT G. BLOCH, Chicago: Dr. Tucker has many more statistics on our observations which we could not show. There was also no time to go into the controversy as to the value of tuberculin case finding programs with x-ray examination alone. We have stated that we doubt the case finding value of tuberculin in the adult. All the x-ray methods have their advantages and disadvantages. We are aware that fluoroscopy has the disadvantage of not providing a permanent record and, furthermore, that it requires special training which not even the average chest specialist has. There needs to be a thorough training in the technic of fluoroscopy as well as in the pathology of the lung, and we ourselves have witnessed programs going on in which, on account of the inexperience of the examiners, the results were not as good as they might have been, and many cases of tuberculosis were missed. A word about the

examinations among students and nurses: One of the objects in presenting this paper was to point out that the medical public and the public at large have been induced to believe in recent years, by a flood of publications from medical schools, universities and hospitals, that tuberculosis is largely a problem of the college student, the medical student and the nurses. This is definitely not so. The incidence of tuberculosis among students and among nurses is not appreciably higher than that in the average population of the same age. Besides, these are very small groups and they are economically and socially good groups. It is needless to say that everything possible should be done to protect students and nurses against the hazards of infection. Beyond that nothing needs to be said about them in public health efforts to find tuberculosis in the general population. The groups in which tuberculosis needs to be looked for primarily are the groups that Dr. Edwards has just presented. With reference to Dr. Haven Emerson's remarks, I should like to say that the sputum examinations among pneumonia patients in Minnesota merely indicate that a lot of tuberculosis is still being misdiagnosed as pneumonia.

Clinical Notes, Suggestions and New Instruments

THE DIAGNOSIS OF HERNIA

STEPHEN A. ZIEMAN, M.D., CHICAGO

In a few weeks the selective service act will be in effect. Inauguration of a selective service brings a new responsibility to the medical profession. The decision as to the ability of any registrant to perform full military service depends on the professional judgment of the local examining physician. Rejec-



Fig. 1.—Usual method of hernial examination as described in textbooks.

tion of the candidate because of physical defect may prove demoralizing to the individual; mistake in diagnosis, costly to the government.

The presence of a hernia in men of the draft age is a deterrent to military service, while the widespread prevalence of hernia in men of this age group necessitates a correct understanding on the part of the physician as to what constitutes a hernia. I consequently propose the following considerations in the hope

that they may be helpful in the diagnosis and differential diagnosis of hernia. Mistake in this matter is less the fault of the examining physician than it is inaccurate surgical teaching on this subject. To instruct the student that an impulse



Fig. 2.—Author's method of examining for hernia, using right hand for right side of patient.

perceptible on coughing or straining while the examining finger is in the external inguinal ring is diagnostic of a hernia is to create a misconception. A little thought on this point will



Fig. 3.—Author's method of examining for hernia, using left hand for left side of patient.

demonstrate the fallacy. The insertion of a finger into the external inguinal ring (fig. 1) produces a cremasteric reflex and consequently the cord structures are retracted or pushed upward by such a procedure, not infrequently without pain. When the patient is now advised to cough, the contraction of this muscle is overcome and a sudden relaxation results in

the production of a thud on the examining finger from the cord structures.

Second, there are cystic and solid tumors, especially lipomatous masses in this region, which undergo a similar contraction owing to the action of the cremasteric muscle, and on its release these tissues may give an impulse and a false impression of a hernia.

Third, the differential diagnosis of hernia is not always an easy matter. Some surgeons challenge its possibility in many instances. To distinguish between a direct, an indirect or a femoral hernia with any degree of accuracy may constitute a surgical problem.

To help correct these conditions, I suggest a method which has proved very encouraging in clarifying these difficulties. The method (fig. 2), in brief, consists in placing the first, second and third fingers over the inguinal region in such a manner that the index finger rests on the so-called weak spot. The middle finger lies along the direction of the inguinal canal with the tip of the finger at the external inguinal ring, while the third finger controls the femoral canal and the fossa ovalis. With the hand in this position it is possible to perceive a peculiar sliding, pushing motion of a viscus under one or

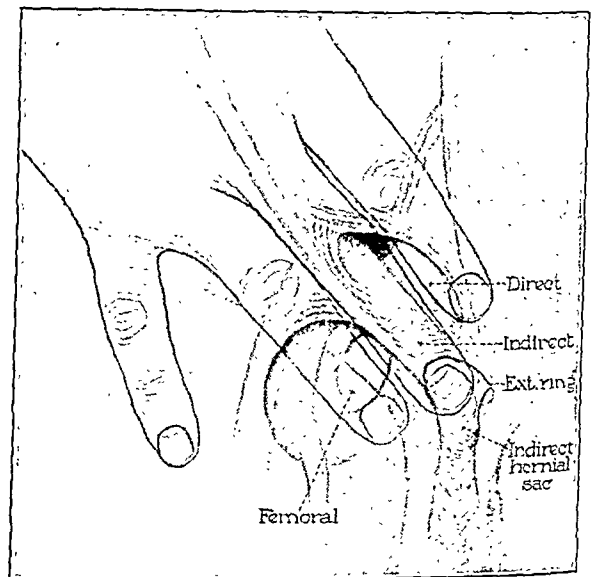


Fig. 4.—Relationship of the various hernias to the examining fingers.

another of the examining fingers when the patient is directed to cough or strain. Thus immediately a direct, an indirect or a femoral hernia is determined. If there is a bulging mass apparent to the eye, the examining hand forces the mass inward and again coughing or straining immediately differentiates the type of hernia present.

The patient is always examined in the upright position with the examiner standing somewhat behind and to the right (figs. 2 and 3), using the right hand for a right inguinal hernia, and to the left, using the left hand for a left inguinal hernia. This method in no way distorts the relationships of the parts in this region and obviates a palpation artefact. A peculiar gurgling, sliding or slipping motion under one or another finger (fig. 4) alone determines the presence of a hernia. The feeling of solid or cystic masses results in an entirely different sensation. I moreover feel that straining is a better method for eliciting the essential diagnostic factor than is coughing.

The diagnosis of a hernia in many cases may be reached on careless inspection, but the method here proposed is particularly helpful in borderline cases, cases of relaxed abdominal muscles or large external inguinal rings. The method, furthermore, has been attested at the operating table, where patients have been operated on and no hernial sac was demonstrable.

30 North Michigan Avenue.

Special Clinical Article

THE SURGICAL TREATMENT OF HYPERTENSION

RESULTS IN 350 CONSECUTIVE CASES TREATED BY
BILATERAL SUPRADIAPHRAGMATIC SPLANCHNI-
CECTOMY AND LOWER DORSAL SYMPA-
THETIC GANGLIONECTOMY

CLINICAL LECTURE AT NEW YORK SESSION

MAX MINOR PEET, M.D.

WARD WILSON WOODS, M.D.

ANN ARBOR, MICH.

AND

SPENCER BRADEN, M.D.

CLEVELAND

The evaluation of any surgical procedure in the treatment of a systemic disease can be reached only after an adequate period of carefully controlled and unbiased trial. This trial demands that certain fundamental conditions be strictly adhered to: 1. The surgical procedure must be utilized in a large number of cases and must remain identical in all cases. 2. The selection of cases must be based on constant criteria, fully investigated in each case before operation. 3. Postoperative results must be judged by the same criteria in an identical manner and on as many occasions as possible. 4. All cases in which operation is performed must be included in the results. 5. The trial must extend over a sufficiently long period of time to eliminate mere temporary effect of the operative procedure.

It is our purpose in this paper to present evidence that the surgical treatment of hypertension has fulfilled the demands of such a trial and consequently should now take its deserved place in the armamentarium of treatment of this disease.

The history of the development of the surgical treatment of hypertension has been reviewed elsewhere.¹ At present four distinct operative procedures are most commonly employed. Their results, studied over a long period of time, must decide the relative merit of each. They are adrenal denervation by celiac ganglionectomy;² subdiaphragmatic, extraperitoneal, bilateral resection of the splanchnic nerves with removal of the upper two lumbar sympathetic ganglions and the intervening chain;³ bilateral transdiaphragmatic removal of the lower dorsal and upper lumbar sympathetic chain with its ganglions and the rami forming the splanchnic nerves,⁴ and bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy.⁵

The last named procedure was first introduced into this country by Peet in 1933 and has been used unaltered by him and his associates at the University of

Michigan Hospital since that time. More than 500 patients have been operated on by the Department of Neurosurgery by means of this technic. The results of the total series are comparable with those presented in this study.

It is not within the scope of this paper to review the experimental work on the etiology of hypertension⁶ nor will an attempt be made to define or classify the disease. Suffice it to say that evidence points to renal ischemia, no matter what the cause, as the usual basic factor in hypertension. The rationale on which we base our operative procedure is therefore the relief of renal ischemia by interruption of the sympathetic vasoconstrictor outflow to the kidneys.

The technic of bilateral supradiaphragmatic splanchnicectomy and dorsal sympathetic ganglionectomy has been described in detail.⁵ Briefly it consists of bilateral paravertebral incisions, usually under avertin with amylene hydrate anesthesia, centering over the eleventh intercostal space. A 4 cm. section of the eleventh rib is removed subperiosteally from a point slightly distal to its articulation with the transverse process of the vertebra. The parietal pleura is retracted, exposing first

TABLE 1.—Sex Distribution

	Number	Per Cent
Males.....	165	47
Females.....	185	53
Total cases.....	350	

TABLE 2.—Age Distribution at Time of Operation

	Number	Per Cent
10 to 19 years.....	3	0.8
20 to 29 years.....	21	6
30 to 39 years.....	90	26
40 to 49 years.....	174	50
50 to 59 years.....	61	17
60 to 69 years.....	1	0.2
Total cases.....	350	

the lower dorsal sympathetic chain with its rami forming the lesser splanchnic nerves, and still deeper the greater splanchnic nerve. A 9 to 13 cm. segment of the latter nerve is resected to its point of entry into the crus of the diaphragm. The sympathetic chain including the tenth, eleventh and twelfth ganglions and the lesser and least splanchnic nerves is next removed, the fibers of the diaphragm being split if necessary. The procedure is performed bilaterally in one stage. The average operative time is about one hour. The postoperative stay in the hospital averages about two weeks.

The selection of cases for operation for hypertension at the University Hospital is based on several relatively simple requirements. The patient is preferably not over 50 years of age, but numerous exceptions have been made. The renal function must be adequate as indicated by a urea clearance of more than 40 per cent of normal and a urine concentration above 1.012. No patient with a blood nonprotein nitrogen of more than 45 mg. per hundred cubic centimeters is accepted. The heart must be compensated and the general physical status of the patient adequate to withstand a major operative procedure. Patients with systolic blood pressures under 200 mm. of mercury are usually not advised to have the operation unless they have had an adequate

From the Department of Neurosurgery, University of Michigan Medical School.

Read in the Surgical Division of the General Scientific Meetings at the Ninety-First Annual Session of the American Medical Association, New York, June 11, 1940.

1. Martin, John: The Surgical Treatment of Hypertension, *Internat. Alstr. Surg.* 67: 419-434, 1938; in *Surg., Gynec. & Obst.*, November 1938.

2. Crile, George: The Surgical Treatment of Hypertension, Philadelphia, W. B. Saunders Company, 1938.

3. Craig, W. M., and Adson, A. W.: Hypertension and Subdiaphragmatic Sympathetic Denervation, *S. Clin. North America* 19: 969-980 (Aug.) 1939.

4. Smithwick, R. H.: A Technic for Splanchnic Resection for Hypertension, *Surgery* 7: 1-8 (Jan.) 1940.

5. Peet, M. M.: The Surgical Treatment of Hypertension, *Proc. California Acad. Med.* 5: 58, 1935-1936; *J. Internat. de Chir.* 5: 1-38 (Jan.-Feb.) 1940.

6. Goldblatt, Harry: Studies on Experimental Hypertension: XII. The Experimental Production and Pathogenesis of Hypertension Due to Renal Ischemia, *Am. J. Clin. Path.* 10: 40 (Jan.) 1940.

trial of conservative medical treatment or unless their symptoms are so severe as to warrant the more radical surgical procedure. We are not yet prepared to recommend splanchnicectomy as a purely prophylactic measure, although we feel that for certain young patients

TABLE 3.—*Distribution of Preoperative Blood Pressure Levels*

Pressure in Mm. of Mercury	Number	Per Cent
Systolic		
90 plus.....	7	2
90 to 100.....	69	20
100 to 120.....	150	43
120 to 140.....	109	31
140 to 170.....	15	4
Diastolic		
155 plus.....	42	12
140 to 154.....	86	25
125 to 139.....	106	30
110 to 124.....	95	27
95 to 109.....	21	6

TABLE 4.—*Subjective Symptomatology at Time of Operation*

	Number	Per Cent
Symptoms present.....	344	98
Symptoms absent.....	6	2
Total cases.....	350	

with a strong hereditary background and the typical hyperlabile type of pressure such a recommendation might be made. No patient is operated on whose hypertension is known to be the result of primary disease of the kidney or other organs. Thus an attempt is made to rule out the following preoperatively: glomerulonephritis, pyelonephritis, pyonephrosis, renal or adrenal tumor, or endocrine disturbances accompanied by hypertension. In other words, patients selected for operation are those suffering from a primary type of high blood pressure for which no organic cause can be found.

Herewith are presented the preoperative and postoperative results in 350 consecutive cases of hypertension in which bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy has been performed by one surgeon (Peet) since 1933. The methods of study and the criteria by which the results have been judged are also presented.

METHODS OF STUDY

Each patient is examined preoperatively in the departments of medicine, ophthalmology, cardiology and roentgenology. Kidney function studies include determination of urea clearance, urine concentration and blood non-protein nitrogen. Pyelograms are now made in all cases presenting the possibility of primary renal disease. A teleroentgenogram checked by an orthodiagram and an electrocardiogram are obtained in each case. Frequent blood pressure determinations are taken by several independent observers and the readings averaged.

Postoperatively the patient is advised to return at definite intervals for check-up examination. Because of financial reasons it has frequently been necessary to have the patient return for such studies at our expense. Funds for this purpose were available through special grants to the department of neurosurgery by Mr. Jeremiah Milbank and the Aaron Mendelson Memorial Trust Fund. Approximately 65 per cent of the 350 patients included in this study have returned for one or more examinations at postoperative periods of from nine months to seven years. Acceptable data in the remaining cases have been obtained through the cooperation of the home physician. In only four of the 350 cases

have we been unable to obtain reliable blood pressure determinations nine months or more postoperatively.

On his return for reexamination the patient was subjected to the following routine: Complete and detailed preoperative histories were personally retaken in order to check all preoperative data as to duration of hypertension, symptomatology and incapacitation. Interval histories were recorded in detail. The patient was reexamined by all departments which had examined him preoperatively, and these departments rendered an opinion as to the comparative progress or regression of the case in respect to their specific specialty. All postoperative statistics have been compiled on these opinions.

The blood pressure was taken at least once with the patient in a sitting position, four determinations being obtained from each arm. Whenever possible this was repeated subsequently. An arithmetical average of the systolic and diastolic readings was taken as the significant figure for that visit. It should be noted that these pressure readings were taken while the patient was ambulatory and under the considerable strain of frequent examinations by various departments as compared to preoperatively, when the pressure readings were usually taken with the patient on a regimen of bed rest.

Following this routine it was possible to obtain on each patient unbiased data and evaluation of the patient's course with regard to blood pressure, symptomatology, incapacitation, condition of the ocular fundus, renal function and cardiac status.

As a result of this comprehensive study, which has extended over a period of nearly seven years, an enormous mass of preoperative and postoperative data has been accumulated. Obviously such a fund of information could not be treated by ordinary methods. As a result, each specific item has been coded on tabulating cards, and the statistical correlations, appearing in the accompanying tables, compiled mechanically.⁷

CRITERIA

In order to evaluate the results of operation in the treatment of hypertension it was found necessary to

TABLE 5.—*Incapacitation at Time of Operation*

	Number	Per Cent
No incapacitation.....	65	22
Slight incapacitation.....	16	5
Moderate incapacitation.....	50	17
Marked incapacitation.....	50	17
Complete incapacitation.....	118	39
Total cases.....	299	

TABLE 6.—*Funduscopy Observations at Time of Operation*

	Number	Per Cent
Normal fundi.....	12	3
	333	97
	144	41
rhages and exudates.....	95	29
(c) Papilledema.....	94	27
Total cases.....	345	

establish certain criteria by which all cases could be judged and from which statistics could be compiled. Obviously these criteria are, to a certain extent, empirical in character and are therefore open to criticism. In order to obviate as much of this criticism as possible, the specialists in each department were asked to estab-

7. Braden, Spencer, and Kahn, E. A.: The Surgical Treatment of Hypertension: A Preliminary Report of Method of Study and Results in 264 Cases, *Yale J. Biol. & Med.* 11: 449-458 (May) 1939.

lish their own criteria of normality and significant change. These criteria are as follows:

Significant reduction in blood pressure is considered as a drop of 40 mm. systolic and 15 mm. diastolic or more from the preoperative level. The blood pressure

TABLE 7.—Keith-Wagener-Craig Classification Funduscope Observations at Time of Operation

	Number	Per Cent
Normal fundi.....	12	3
Group 1.....	15	4
Group 2.....	77	23
Group 3.....	147	43
Group 4.....	94	27
Total cases.....	345	

TABLE 8.—Cardiac Status at Time of Operation

	Number	Per Cent
A. Electrocardiographic Observations		
Normal electrocardiogram.....	85	38
Abnormal electrocardiogram.....	137	62
Total cases.....	222	
B. Teleoroentgenographic Observations		
Normal cardiac size (average: +5%).....	110	51
Cardiac enlargement (average: +35%).....	105	49
Total cases.....	215	

value given for each postoperative check-up is the arithmetical average of all readings by the departments of medicine and neurosurgery. No pressure is considered significantly reduced unless both the systolic and diastolic values are lowered.

Marked reduction in blood pressure is considered as a drop of 80 mm. systolic and 25 mm. diastolic, or more.

Reduction of blood pressure to normal is considered as a drop to, or lower than, 130 mm. systolic and 90 mm. diastolic for patients up to the age of 40. After the age of 40 the drop must be to, or lower than, 150 mm. systolic and 100 mm. diastolic.

Changes in ocular fundi are evaluated by the department of ophthalmology. Improvement of the pathologic vessel changes, in the number of hemorrhages and exudates, of angiospasm and of papilledema is noted only when the change is beyond dispute. All fundi with equivocal changes are regarded as unchanged. Cases in which papilledema disappeared after operation have been given special attention. In addition the Keith-Wagener-Craig classification is used.

Urine concentration is regarded as normal if the patient is able to concentrate to a specific gravity of 1.029 or higher after thirty-eight hours without water, on a dry diet. During the past year, because of inconvenience of this test to the patient, a short concentration test has been substituted in which the normal value is considered to be 1.026 following eighteen hours without food or fluids. In both tests a change in specific gravity of three points or more is deemed necessary in order to be considered significant.

Urea clearance is considered normal if the values of the test averaged 75 per cent or higher. A change of 15 per cent is considered significant.

Cardiac size is determined by the teleoroentgenogram. Fifteen per cent above the predicted normal cardiac area is taken as evidence of enlargement. A change of 10 per cent or more is considered significant. All teleoroentgenographic measurements have been checked by orthodiagram.

Electrocardiograms are evaluated by the cardiologists on the degree of axis deviation and T wave changes. Each postoperative reading has been compared with the one taken preoperatively.

Symptomatology is, by necessity, evaluated from the patient's own statement. An attempt is always made to have all information as to changes in symptoms offered voluntarily by the patient.

Incapacitation is judged on the basis of the amount of work the patient was able to do immediately prior to operation as compared with his working ability before the onset of any incapacitation. Postoperative changes are judged on a similar basis.

In each instance the evaluation in every phase of the investigation has been made with the cooperation of the respective participating specialist. This approach has seemed, as nearly as possible, to avoid all individual prejudice. In the data presented it will be noted that in certain phases the proportion of cases without pertinent information may seem high. The primary reason is that whenever it has seemed apparent that the available data were incomplete or possibly inaccurate they have been deleted, even though such data indicated favorable results.

PREOPERATIVE STATISTICS

The 350 patients included in this study were operated on consecutively from November 1938 to September 1939. The technic of operation as described was used exclusively, and the operation was performed in each case by the same surgeon (M. M. P.). In tables 1 to 9 the preoperative observations are presented and discussed.

Approximately an equal percentage of males and females were operated on (table 1).

Ninety-three per cent of the patients were 30 years of age or older, with 50 per cent in the fifth decade (table 2).

TABLE 9.—Renal Function at Time of Operation

	Number	Per Cent
A. Urine Concentration		
Normal urine concentration.....	55	16
(Average: 1.032)		
Decreased urine concentration.....	279	84
(Average: none obtained *)		
Total cases.....	331	
B. Urea Clearance		
Normal urea clearance.....	191	56
(Average: 95%)		
Decreased urea clearance.....	148	41
(Average: 51%)		
Total cases.....	339	

* See under "Criteria."

TABLE 10.—Postoperative Study

Total patients operated on from 1933 to September 1939.....	350
Total cases studied in one or more phases postoperatively.....	316
Total cases with insufficient data in any postoperative phase....	4
Total deaths	107
Operative deaths	12
Subsequent deaths	95
(a) Due directly to hypertension.....	77
(b) Due to other causes.....	5
(c) No data	13
Operative mortality	(3.4%)

The blood pressure levels indicate a marked degree of hypertension in these patients. The average level is 218/133. Sixty-five per cent have systolic pressures above 210 mm. and 77 per cent have diastolic pressures above 125 mm. (table 3). These figures become even more significant when it is realized that these pressures were usually taken in the hospital with the patient on

bed rest and, commonly, following strict medical treatment over an extended period of time.

In the majority of cases the symptoms present (table 4) were severe. In the order of frequency they were occipital headache, headache elsewhere, increased nervousness and irritability, ease of fatigue, urinary frequency and nocturia, dizziness, dulness of mental processes, dyspnea, blurring of vision, nausea and vomiting, hemiplegia.

Exact information as to incapacitation (table 5) was available in 299 cases. It is significant that in 56 per cent of the cases studied incapacitation was either complete or marked, another indication that the hypertension level of the group was high.

Exact information as to the preoperative condition of the fundi (table 6) was not available in only five cases. It is significant that the hypertension was of severity sufficient to cause fundus changes in 97 per cent of the cases and that of these 56 per cent showed hemorrhages and exudates or papilledema.

Exact information as to fundusoscopic examination (table 7) was not available in five cases. It is significant that 70 per cent of the cases studied were in groups 3 and 4, i. e. showed, according to the authors of the classification, a marked severity of the hypertensive process and a very poor prognosis.

TABLE 11.—Distribution of Follow-Up Studies of 350 Cases According to Operative Year

Year of Operation	Number of Patients	Dead Before 9 Mos.	Cases Studied 9 Mos. or More Postoperatively (Including Deaths After 9 Mos.)	Cases with No Data in Any Phase (Including Deaths After 9 Mos.)
1933.....	1	..	1	..
1934.....	32	8	24	..
1935.....	62	7	54	1
1936.....	59	11	46	2
1937.....	93	10	83	..
1938.....	59	4	55	..
1939.....	44	4	39	1
Totals.....	350	44	302	4

Acceptable data were obtained on electrocardiographic examination in 222 cases, and on teleoroentgenographic measurement in 215 cases (table 8). Cardiac damage was indicated in about 60 per cent of the cases and enlargement in nearly 58 per cent. It is significant that the average percentage of enlargement above predicted normal was 35.

Exact information on urine concentration (table 9) was not available in sixteen cases and on urea clearance in eleven cases. Renal damage, as measured by urine concentration, occurred in 84 per cent of the cases, the extent indicated by the low average figure of 1.023.

Urea clearance was diminished in only 44 per cent. In these cases, however, the average value of 51 per cent indicates that the damage to the kidneys was fairly severe.

In summary of the preoperative observations in 350 cases it can be said that the hypertension (averaging 218/133) of the whole group was high. This fact is confirmed by the high percentage of severe ocular fundus changes (70 per cent in Keith-Wagoner-Craig groups 3 and 4) and of renal and cardiac damage. Almost all the patients (98 per cent) had symptoms sufficiently severe to cause complaint. In 39 per cent incapacitation was complete.

POSTOPERATIVE STATISTICS

Of the 350 patients operated on for hypertension approximately 65 per cent have been reexamined postoperatively in the clinics of the University Hospital and

34 per cent have had acceptable data forwarded by their local physician or hospital. Only four patients (1 per cent) have not presented information in at least one phase.

The data collected cover a time period of approximately seven years. No case has been included that has not had at least a nine months postoperative period.

TABLE 12.—Blood Pressure

	Number	Per Cent
Cases studied 9 months or later postoperatively (including deaths).....	290	100
Reduced (more than 40 mm. systolic and 15 mm. diastolic).....	149	51.4
Unchanged.....	134	46.2
Increased (more than 10 mm. systolic and 5 mm. diastolic).....	7	2.4
Cases with no data or dead before 9 months postoperatively.....	60	

If the sixty patients concerning whom no data were obtained or who died before nine months are considered as unchanged or worse, the percentage of patients with significantly reduced blood pressure in the whole group of 350 cases becomes 42.6.

This was deemed necessary to obviate the criticism that improvement was only temporary following a major operative procedure. The majority of patients have been reexamined more than once, and frequently at yearly postoperative intervals.

In evaluating the results of the operation those patients who have died subsequent to nine months after operation (obviously the poorest results) have been included in the complications.

Statistics are presented for each separate phase of the postoperative examination. Each phase is dealt with by two methods: first, a summary is given of the best results recorded at any one examination made nine months or more after operation, regardless of the exact postoperative interval; second, a table is presented which demonstrates the results by postoperative years.

No selection of cases was made. All who were able to return did so. More difficulty was encountered in getting the well patient who was working full time, and who had no complaints, to return than the sick patient, who was more than willing to take advantage of the opportunity of the gratis examination.

TABLE 13.—Analysis of Patients with Significantly Reduced Blood Pressure

	Number	Per Cent
Number of cases studied.....	149	100
Reduced to normal..... (130/90 for ages 20 to 40) (150/100 for ages 40 to 70)	56	37.5
Markedly reduced (but not to normal)..... (More than 80 mm. systolic and 25 mm. diastolic)	15	10.1
Reduced (but not markedly or to normal)..... (More than 40 mm. systolic and 15 mm. diastolic)	78	52.4

Thus, of those cases in which there was significantly reduced blood pressure 47.6 per cent were reduced to normal, markedly reduced or both.

All except 1 per cent of the cases have been studied in one or more phases postoperatively (table 10). The operative mortality was 3.4 per cent. Further statistical study of the deaths appears in a separate section later.

CLINICAL RESULTS OF SPLANCHNICECTOMY

No cases have been included (table 11) that have not been studied nine months or more from the time of operation. It is seen that seventy-eight cases have been studied more than five years and 196 cases for more than three years. With this wide spread of postoperative information it will be possible to show that the effects of the operation are not temporary.

Only 2.4 per cent of the 290 cases in which reliable postoperative information was obtained (table 12) showed a steady increase in blood pressure. It is obvious, therefore, that the majority of those patients who subsequently died had, at least at one examination, a blood pressure that was either improved or unchanged; otherwise the percentage would be much higher. It is only fair, however, to assume that the forty-four patients who died before nine months had no decrease in blood pressure. To be absolutely fair the sixteen patients on whom no data were obtained are also considered to be worse, although they undoubtedly were distributed in the same fashion as the others. Thus the absolute minimum of cases showing a significant reduction in blood pressure becomes, as noted, 42.6 per cent. Table 12 offers no information as to what period after nine months postoperatively the reduction occurred or whether it was maintained.

period of time without relief of either symptoms or high blood pressure. The operation was, then, a court of last appeal.

Table 14 is a demonstration of maintenance of the results of splanchnicectomy over a period of years. A sufficient number of the patients operated on were able to return for one or more check-up examinations through the years to show that reduction in blood pressure, once attained, persists. It is of equal importance to note that there was no significant increase in the percentage of patients in whom the blood pressure grew worse. It should be remembered that these statistics include check-up examinations of patients who subsequently died.

It may be assumed that if a patient had a significantly reduced blood pressure at, for example, the fifth year check-up the reduction had been maintained over that period. It is seen, as in the summary of check-up

TABLE 14.—Blood Pressure per Postoperative Year and Analysis of Patients with Significantly Reduced Blood Pressure per Postoperative Year

	First Year (9 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.).....	202	135	105	48	37	7	1
Blood pressure increased.....	3%	4%	4%	6%	5%
Blood pressure unchanged.....	33%	50%	40%	38%	49%	37%
Blood pressure reduced.....	44%	46%	50%	56%	46%	43%	100%
Analysis of reduced blood pressures.....	89	62	51	27	17	3	1
Reduced to normal..... (130/90 for ages 20 to 40; 150/100 for ages 40 to 70)	19%	34%	40%	26%	24%	33%
Markedly reduced (80 mm. systolic and 25 mm. diastolic, but not to normal)	20%	16%	18%	7%	24%	33%	100%
Reduced (40 mm. systolic and 15 mm. diastolic, but not markedly or to normal)	61%	50%	42%	67%	52%	33%

The arbitrarily chosen criteria (table 13) for "normal," "markedly reduced" and "reduced" blood pressures are obviously open to criticism. They were established only after much discussion and collaboration with well qualified observers in the field of hypertension, and then only for the purpose of simplifying the data. It is felt, however, that since the postoperative pressures were all taken with the patients ambulatory and under a considerable mental and physical strain, as compared to the preoperative readings when the patients had usually been on bed rest, the reductions are of true significance. Thus, as already noted, nearly 50 per cent of the patients who had reduced blood pressures showed a drop to normal, a marked reduction or both.

TABLE 15.—Age Distribution Correlated with Postoperative Blood Pressures

Number of cases studied 9 months or more postoperatively (including deaths)	Total Cases Studied			
Age at Time of Operation	Total Cases Studied	Reduced	Unchanged	Increased
10 to 19 years.....	1	1 (100%)		
20 to 29 years.....	18	14 (78%)	4 (22%)	
30 to 39 years.....	74	38 (51.4%)	35 (47.3%)	1 (1.3%)
40 to 49 years.....	150	74 (49.3%)	71 (47.3%)	5 (3.3%)
50 to 59 years.....	46	22 (48%)	23 (50%)	1 (2%)
60 years plus.....	1	1 (100%)		
Totals.....	290	149 (51.4%)	134 (46.2%)	7 (2.4%)

No other form of therapy as yet reported has shown as great a percentage of cases in which the blood pressure has been reduced to this extent.

This fact becomes even more significant when it is realized that the majority of these patients had been thoroughly treated by medical means over an extended

examinations showing the best results (tables 12 and 13), approximately 50 per cent of the patients show a reduction in blood pressure no matter whether the postoperative period was one or five years. Obviously the total number studied yearly reduces as the number operated on that number of years ago grows smaller.

TABLE 16.—Eyeground Changes

Total patients studied preoperatively and postoperatively..... 219			
Postoperative Result			
Preoperative Status	Improved	Unchanged	Worse
Normal eyegrounds..... 10	10 (100%)
Abnormal eyegrounds..... 209			
(a) Abnormal vessels only..... 102	50 (49%)	44 (43%)	8 (8%)
(b) Abnormal vessels plus hemorrhages and exudates..... 65	57 (88%)	6 (9%)	2 (3%)
(c) Papilledema..... 42	38 (91%)	4 (9%)	
	7 (17%) diminished		
	31 (74%) absent		

In analyzing those patients with reduced pressures it becomes clear that the degree of reduction, i. e. markedly reduced, reduced to normal or both, is also maintained throughout the postoperative years.

In table 15 the remarkable consistency of the percentage distributions is seen again. Surprisingly enough there is little evidence that older patients have a poorer prognosis as to the result of splanchnicectomy than do relatively younger patients. The best prognosis for reduction in blood pressure is in the age group from 10 to 29 years (78 per cent). After this age no significant difference is seen in the percentage with reduced pressure (always in the neighborhood of 50 per cent of the cases studied).

Table 16 indicates in each case studied nine months or more postoperatively the most favorable effect of the operation on the fundus oculi at any one examination.

It is significant that only ten patients of the 219 with fundusoscopic examinations both preoperatively and postoperatively showed a steady progression of the damage to the fundi, whereas 145 patients showed definite improvement regardless of the degree of damage before operation.

One of the most remarkable results of the operation occurred in the forty-two cases in which papilledema was present on preoperative examination. Of these patients thirty-one, or 74 per cent, showed complete disappearance of the edema on one or more postoperative examinations. Seventeen per cent showed diminution in the edema, 9 per cent remained unchanged and none grew steadily worse. Again it must be remembered that patients who subsequently died were included in these statistics.

65 to 100 per cent. In other words, the disappearance of the edema, when it occurred, was not a temporary effect since the percentage was approximately the same no matter what year the patient returned for his reexamination.

Of the 219 patients studied (table 18) both preoperatively and postoperatively (nine months or more after operation) only ten patients, or 4 per cent, had normal fundi preoperatively, and only sixty-three patients, or 29 per cent, showed the milder changes of groups 1 and 2.

The greatest number (147, or 67 per cent) had the advanced changes of groups 3 and 4, i. e. angiospasm or papilledema or both. Yet it was in the latter groups that the greatest improvement occurred as the result of operation. Thus 80 per cent of those who had group 3 preoperatively showed improvement on at least one examination postoperatively and, as shown in table 16, 91 per cent of group 4 showed improvement. Again it

TABLE 17.—Fundus Changes per Postoperative Year

	First Year (9 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.).....	136	91	72	38	23	6	1
Abnormal preoperatively							
Abnormal vessels only preoperatively.....	65	46	41	22	13	2
Postoperatively partially improved.....	43%	43%	61%	41%	61%
Postoperatively unchanged.....	48%	46%	46%	45%	31%	100%
Postoperatively worse.....	9%	9%	3%	14%	8%
Abnormal vessels plus hemorrhages and exudates preoperatively.....	37	30	16	7	5	2
Postoperatively partially improved.....	86%	80%	87.5%	71%	80%	50%
Postoperatively unchanged.....	14%	13%	12.5%	29%
Postoperatively worse.....	7%	20%	50%
Papilledema.....	26	14	13	7	5	2	1
Postoperatively absent.....	73%	65%	85%	100%	100%	100%	100%
Postoperatively partially improved.....	12%	28%	15%
Postoperatively unchanged.....	15%	7%
Postoperatively worse.....
Normal preoperatively.....	8	4	2	2
Postoperatively continues normal.....	100%	75%	100%	100%
Postoperatively worse.....	25%

Criticism could be made of the results recorded in table 16 on the ground that the results were only temporary and were not maintained. The table makes such criticism untenable, since it can be seen that the percentages, whether indicating good or bad results, remain relatively the same throughout the postoperative years.

TABLE 18.—Eyegrounds (Keith-Wagener-Craig Classification)

Preoperative Status		Postoperative Status		
		Improved	Unchanged	Worse
Total patients studied preoperatively and postoperatively.....		219		
Abnormal eyegrounds 209				
Group 1.....	13	1 (7%)	10 (78%)	2 (15%)
Group 2.....	50	22 (44%)	25 (50%)	3 (6%)
Group 3.....	105	84 (80%)	15 (15%)	5 (5%)
Group 4.....	42	7 (17%)	4 (9%)
Normal eyegrounds... 10		(absent) 31 (74%)	10 (100%)

Thus, about 45 per cent of the patients who had abnormal vessels only, i. e. showed sclerosis or angiospasm or both, maintained partial improvement throughout. Similarly, approximately 80 per cent of those with abnormal vessels, hemorrhages and exudates demonstrated a maintenance of improvement.

It is significant that the percentage of patients who had complete disappearance of papilledema following operation ranged through the postoperative years from

should be noted that of the latter group 74 per cent had complete disappearance of their papilledema at one or more examinations.

In a subsequent paper, now being prepared, it will be shown that the prognosis following splanchnicectomy for patients of groups 3 and 4 is far better than that given by the authors of this classification for the same groups treated only by medical means.

Once again (table 19), as in table 17, it is seen that improvement in eyegrounds is not a temporary effect of splanchnicectomy but rather that the percentages remain remarkably constant no matter what the year of check-up. Also it is again demonstrated that the greatest percentage of improvement occurs in those with the most serious damage to the fundi—i. e. in groups 3 and 4, and that this improvement is maintained proportionally throughout the years. It should be kept in mind that these statistics include, as has already been pointed out, the postoperative examinations of those patients who subsequently died; in other words, the cases with the poorest results.

The average heart size of the 105 patients (table 21) before operation was +18 per cent. Following operation, on at least one examination nine months or more postoperatively, the average heart size was reduced to 8.9 per cent.

It is significant that of the fifty patients who had hearts enlarged before operation 50 per cent returned to normal postoperatively and 14 per cent were partially improved. Only 4 per cent grew steadily worse.

Ninety-three per cent of the patients with normal heart size preoperatively remained within normal limits postoperatively.

preoperatively had an abnormal recording postoperatively.

The significant finding is that only five cases out of 127 demonstrated steadily increasing cardiac damage as measured by electrocardiogram.

The arrest in cardiac damage as measured by the electrocardiogram (table 23) was not a temporary effect

TABLE 19.—*Fundus Changes per Postoperative Year (Keith-Wagener-Craig Classification)*

	First Year (9 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied.....	136	94	72	38	23	6	1
Abnormal preoperatively							
Group 1	8	5	4	2	4	1
Postoperatively partially improved.....	1 (12.5%)	1 (25%)	1 (25%)
Postoperatively unchanged	5 (62.5%)	5 (100%)	3 (75%)	2 (100%)	2 (50%)	1 (100%)
Postoperatively worse	2 (25%)	1 (25%)
Group 2	33	26	13	8	1
Postoperatively partially improved	13 (39%)	10 (38%)	4 (31%)	1 (12.5%)	1 (100%)
Postoperatively unchanged	19 (58%)	13 (50%)	8 (61%)	5 (62.5%)
Postoperatively worse	1 (3%)	3 (12%)	1 (8%)	2 (25%)
Group 3	61	45	40	19	13	3
Postoperatively partially improved	45 (74%)	30 (67%)	30 (75%)	14 (74%)	10 (77%)	1 (33.3%)
Postoperatively unchanged	14 (23%)	12 (27%)	9 (22.5%)	3 (16%)	1 (8%)	1 (33.3%)
Postoperatively worse	2 (3%)	3 (6%)	1 (2.5%)	2 (10%)	2 (15%)	1 (33.3%)
Group 4	26	14	13	7	5	2	1
Postoperatively papilledema absent	19 (73%)	9 (65%)	11 (85%)	7 (100%)	5 (100%)	2 (100%)	1 (100%)
Postoperatively papilledema partially improved.....	3 (12%)	4 (28%)	2 (15%)
Postoperatively papilledema unchanged	4 (15%)	1 (7%)
Normal preoperatively	8	4	2	2
Postoperatively continues normal.....	8 (100%)	3 (75%)	2 (100%)	2 (100%)
Postoperatively worse	1 (25%)

TABLE 20.—*Heart Size per Postoperative Year*

	First Year (9 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.)	65	43	30	12	8	2
Heart enlarged preoperatively.....	30	24	13	8	6	1
Postoperatively normal.....	53%	29%	39%	50%	17%	100%
Postoperatively improved	7%	38%	15%	33%
Postoperatively unchanged	37%	29%	46%	50%	50%
Postoperatively further enlarged	3%	4%
Heart normal size preoperatively.....	35	19	17	4	2	1
Postoperatively continues normal	94%	93%	82%	100%	100%	100%
Postoperatively enlarged	6%	5%	8%

Diminution in heart size postoperatively was not a temporary effect of splanchnicectomy (table 20). Thus there is relatively constant distribution of the percentages no matter at what postoperative period the check-up examination was made.

Of seventy-three patients who had abnormal electrocardiograms before operation (table 22) 29 per cent

of splanchnicectomy. The percentages of the patients at each yearly check-up are relatively constant no matter the postoperative time interval. The marked increase

TABLE 22.—*Electrocardiogram*

Total patients studied preoperatively and postoperatively..... 127				
Postoperative Result				
Preoperative Status	Normal	Partially Improved	Unchanged	Worse
Electrocardiogram				
Abnormal, 73 cases.....	21 (29%)	18 (25%)	30 (41%)	4 (5%)
Normal, 54 cases.....	53 (95%)	1 (2%)

TABLE 21.—*Heart Size (Measured by Telcorontgenogram and Expressed in Percentage Above Predicted Normal Area)*

Total patients studied preoperatively and postoperatively..... 103				
Postoperative Result (Average Size: +8.9%)				
Preoperative Status (Average Size: +18%)	Normal	Partially Improved*	Unchanged	Further Enlarged
Heart enlarged preoperatively, 60 cases (15% above predicted normal area).....	50%	14%	32%	4%
Heart size normal preoperatively, 53 cases.....	93%	7%

* A change of 10 per cent is considered significant.

became normal, 25 per cent were partially improved and 41 per cent remained unchanged. Only one patient out of fifty-four having a normal electrocardiogram

at the sixth year check-up is probably apparent (only three cases studied) rather than real.

Urea clearance determinations were made in 189 cases (table 25) before operation and at least once nine months or more postoperatively. Only 7 per cent of those with preoperatively abnormal values and 13 per cent of those with preoperatively normal values showed a steady decrease in renal function postoperatively. It is of importance to note that 51 per cent of the sixty-

nine cases showing decreased renal function before operation returned to normal or were partially improved postoperatively.

Table 24 would indicate that improvement in renal function as measured by urea clearance is not a temporary result of splanchnicectomy but persists in an almost constant percentage of cases over a long postoperative period. Similarly the percentages of those whose renal function grew worse following operation also remains nearly constant instead of increasing through the years as would be expected had the patients not been operated on.

Urine concentration tests were made in 208 cases (table 26) both preoperatively and postoperatively (at least once nine months or more after operation). Of

demonstrated by the consistency of the percentages showing improvement or return to normal throughout the postoperative years. Poorest results are seen in those patients who had normal concentrating ability preoperatively.

Of 284 patients 277 (98 per cent) complained of symptoms due to hypertension. Of these 86 per cent stated, on at least one examination nine months or more postoperatively, that their symptoms had either completely disappeared or were improved. Only 3 per cent were worse. Of the seven patients who had no symptoms before operation only one developed persistent symptoms. Deducting a possible psychotherapeutic effect, it still remains obvious that the majority of patients benefited markedly from the operation.

TABLE 23.—*Electrocardiogram per Postoperative Year*

	First Year (0 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.).....	73	49	37	15	10	5
Electrocardiogram abnormal preoperatively.....	37	30	17	10	7	3
Postoperatively normal.....	24%	23%	35%	40%	43%	33.3%
Postoperatively partially improved.....	33%	17%	23%	10%	14%
Postoperatively unchanged.....	38%	33%	30%	40%	20%	33.3%
Postoperatively worse.....	5%	7%	12%	10%	14%	33.3%
Electrocardiogram normal preoperatively.....	36	19	20	5	3	2
Postoperatively continues normal.....	97%	100%	100%	100%	100%	100%
Postoperatively abnormal.....	3%

TABLE 24.—*Urea Clearance per Postoperative Year*

	First Year (0 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.).....	116	87	58	31	22	6	1
Abnormal preoperatively.....	52	31	17	11	7	2
Postoperatively normal.....	33%	48%	33%	64%	43%	50%
Postoperatively improved.....	4%	6%	14%
Postoperatively unchanged.....	42%	36%	47%	18%	43%	50%
Postoperatively worse.....	15%	10%	18%
Normal preoperatively.....	64	56	41	20	15	4	1
Postoperatively continues normal.....	78%	78%	78%	70%	87%	75%	100%
Postoperatively abnormal.....	22%	21%	22%	30%	13%	25%

those who had decreased concentrating ability, 27 per cent returned to normal after operation and an additional 17 per cent were partially improved, making a total of 44 per cent improved.

It should be explained that the concentration test was shortened to eighteen hours during the last year of the study. It seems probable that the higher percentage of patients failing to show improvement in this

Complete or partial relief of the symptoms was maintained, as shown by the relative consistency of the percentages over a long period of time (table 28). It is

TABLE 25.—*Renal Function*

Urea Clearance				
Total patients studied preoperatively and postoperatively..... 181				
Postoperative Result				
Preoperative Status	Normal	Partially Improved	Unchanged	Worse
Decreased (below 75%) 69 cases.....	31 (45%)	4 (6%)	29 (42%)	5 (7%)
Normal (75% or above) 112 cases.....	97 (87%)	15 (13%)

phase is due to the fact that the results on this shorter test are not exactly comparable with those on the longer test.

Improvement in renal function as indicated by urine concentration tests is maintained (table 27). This is

TABLE 26.—*Renal Function*

Urine Concentration				
Total patients studied preoperatively and postoperatively..... 208				
Postoperative Result				
Preoperative Status	Normal	Partially Improved	Unchanged	Worse
Decreased, 172 cases..... (Long test: below 1.029) (Short test: below 1.026)	47 (27%)	30 (17%)	70 (41%)	25 (15%)
Normal, 36 cases..... (Long test: 1.029 plus) (Short test: 1.026 plus)	23 (64%)	13 (36%)

important to note the low percentages of those who remained unchanged or who grew worse.

It is obvious from these large percentages showing complete relief or partial improvement that many of the patients did not have a corresponding diminution in blood pressure. Many of the patients had blood pressures unchanged by operation. To them, however, the relief of symptoms, usually headache, was of vital importance. The answer to this apparent paradox is not

available at present. Research is being carried on by one of us (W. W. W.) relative to the physiology of cerebrospinal fluid pressure relationships in an attempt to explain why, following operation, so many patients receive persistent symptomatic relief from their headaches even though their blood pressure continues unchanged or goes even higher.

The statistics in table 30 indicate one of the most important results of splanchnicectomy. To the patient who must earn his living the ability to return to gainful occupation is of primary importance. Thus, of eighty-four patients who were completely incapacitated before operation 51 per cent had returned to full-time work at the time of at least one examination nine months or more postoperatively; 23 per cent had returned to part-time occupation.

percentages are significantly greater than could be expected for patients treated by medical means alone. They become even more significant when the preoperative observations presented in tables 1 to 10 are reviewed, indicating the marked degree of hypertension and the extensive systemic damage present in the majority of these patients before operation.

Wagener and Keith in a recent review of 219 cases of hypertension treated by medical means alone found a survival of only 9 per cent after five to nine years. In our series approximately 50 per cent have survived five years or longer. A paper is now being prepared which will show that the degree of hypertension in our cases as indicated by fundusoscopic examination was of comparable severity to that of the cases collected by these authors.

TABLE 27.—Urine Concentration per Postoperative Year

	First Year (9 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.).....	121	95	72	35	25	7	1
Abnormal preoperatively	96	81	61	30	20	6	1
Normal postoperatively	23%	21%	21%	23%	5%	17%
Improved postoperatively	16%	24%	18%	17%	25%	50%	100%
Unchanged postoperatively	50%	40%	40%	40%	60%	33%
Worse postoperatively	11%	12%	21%	20%	10%
Normal Preoperatively	25	14	11	5	5	1
Continues normal postoperatively.....	64%	57%	36%	20%	40%
Abnormal postoperatively	36%	43%	64%	80%	60%	100%

TABLE 28.—Symptomatology per Postoperative Year

	First Year (9 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.).....	198	132	105	45	36	7	1
Symptoms present preoperatively.....	193	129	104	43	36	7	1
Postoperatively absent	25%	28%	41%	37%	53%	71%	100%
Postoperatively improved	67%	59%	47%	49%	33%	29%
Postoperatively unchanged	11.5%	9%	8%	9%	8%
Postoperatively worse	0.5%	4%	4%	5%	6%
Symptoms absent preoperatively.....	5	3	1	2
Postoperatively unchanged	100%	67%	100%	50%
Postoperatively present	33%	50%

Of even greater significance is the fact that only fifteen of the 244 patients having adequate data on this phase showed a steady increase in their incapacitation. By far the majority showed a complete absence or partial improvement of this symptom.

It is clearly demonstrated in table 31 from the consistently high percentages of those patients, preoperatively incapacitated, who were able, after operation, to carry on full-time work that the effects of splanchnicectomy are not temporary. Thus, for example, 62 per cent of the patients, previously incapacitated, who were studied five years after operation were back at full time

It should be noted, as stated in table 32, that operative deaths, deaths due to causes other than hypertension, and cases in which no data could be obtained are all calculated statistically to give the absolute minimal survival percentages.

TABLE 30.—Incapacitation

Total patients studied preoperatively and postoperatively..... 211		Postoperative Result			
Preoperative Status	Incap. Absent	Partially Improved	Unchanged	Worse	
Incapacitation present 182	101 (55%)	47 (26%)	29 (16%)	5 (3%)	
Slight..... 16	10 (6%)	2 (12%)	4 (25%)		
Moderate..... 43	27 (63%)	11 (26%)	1 (2%)	4 (9%)	
Marked..... 39	21 (54%)	11 (28%)	6 (15%)	1 (3%)	
Complete..... 84	43 (51%)	23 (28%)	18 (21%)		
Incapacitation absent. 62	52 (84%)	10 (16%)	

TABLE 29.—Subjective Symptomatology

Total patients studied preoperatively and postoperatively..... 284		Postoperative Result			
Preoperative Status	Absent	Improved	Unchanged	Worse	
Symptoms present.... 277	109 (39%)	131 (47%)	30 (11%)	7 (3%)	
Symptoms absent 7	6 (86%)	1 (14%)	

work, and an additional 24 per cent were partially improved. The purely economic value of the operation to these patients was obviously very great.

The percentages of survivals according to year of operation are presented in table 32. We believe these

OPERATIVE AND POSTOPERATIVE DEATH STATISTICS

Out of the total number of 350 patients studied, on whom splanchnicectomy was performed, 107 patients died subsequently over a period of nearly seven years. Twelve of these were operative deaths, i. e. death occurred before they left the hospital. Seventy-seven are known to have died subsequently from a cause directly attributable to hypertension. Five are known

to have died from causes other than hypertension. Thirteen are known to be dead but the cause of death is unknown.

The operative mortality attendant on splanchnicectomy was 3.4 per cent. Of the twelve operative deaths ten patients were males and two females. One patient died on the operating table, probably of cerebral embolus. Four patients died immediately after operation (within eight hours), two of these of acute cardiac failure, one of cerebral hemorrhage and one of acute cerebral edema, of unknown etiology. The remaining seven patients died from one to twenty-five days after operation. Three of these died from cerebral hemorrhage, one from myocardial infarction (possibly occurring just before operation), one from pontile thrombosis, one from either coronary occlusion or pulmonary embolus, and one from lobular pneumonia with fibrinopurulent mediastinitis. It is interesting to note that only one patient died of thrombosis of the cerebral vessels, a contingency that would be expected to occur much more often, owing to the marked drop of blood

Data on subjective relief of symptoms were available for eighty-two patients of the total of ninety-five who died subsequent to operation. Following discharge from the hospital and up to the terminal illness, 11 per cent of these patients received complete relief from symptoms, 61 per cent received partial relief, 20 per cent were unchanged and only 6 per cent grew steadily worse. In other words 72 per cent of the patients received either complete or partial relief of their symptoms following operation regardless of the postoperative interval before death or the duration of their terminal illness.

Seventy-five patients died nine months or more following operation. Of these, prior to their terminal illnesses, 23 per cent had significant reduction in blood pressure on at least one examination, 2 per cent had reduction to normal, 63 per cent were unchanged and 12 per cent grew steadily worse.

It is of interest to note that the average postoperative survival period (exclusive of the operative deaths) was nineteen months.

TABLE 31.—*Incapacitation per Postoperative Year*

	First Year (9 to 18 Mos.)	Second Year (18 to 30 Mos.)	Third Year (30 to 42 Mos.)	Fourth Year (42 to 54 Mos.)	Fifth Year (54 to 66 Mos.)	Sixth Year (66 to 78 Mos.)	Seventh Year (78 to 90 Mos.)
Total patients studied (including deaths after 9 mos.).....	171	112	95	43	34	8	1
Incapacitation present preoperatively.....	134	86	81	36	29	8	1
Postoperatively absent	40%	59%	63%	56%	62%	87.5%	100%
Postoperatively partially improved	39%	26%	26%	30%	24%
Postoperatively unchanged	16%	12%	10%	14%	7%	12.5%
Postoperatively worse	5%	3%	2%	7%
Incapacitation absent preoperatively.....	37	26	14	7	5
Postoperatively continues absent	92%	81%	79%	86%	100%
Postoperatively present	8%	19%	21%	14%

pressure which occurs frequently during and immediately after operation.

The sex distribution of mortality is extremely interesting. Far more males died following operation than did

TABLE 32.—*Survival*

Year of Operation	Patients Operated On	Years After Operation	Patients Living	Per Cent Living	No Data
1933.....	1	7	1	100	..
1934.....	32	6	13	40.6	..
1935.....	62	5	37	59.5	1
1936.....	59	4	31	54.2	1
1937.....	93	3	70	75.3	..
1937.....	59	2	50	84.7	..
1938.....	59	1	38	64.4	1
1939 to September..	44	1	38	86.4	1
	350		250	77.7	3

These figures include twelve patients who died as the result of operation and at least five patients dead from causes other than hypertension. The three patients on whom no data were obtained are also calculated as dead.

females. Thus ten males had operative deaths and only two females. Subsequently sixty-four males died (39 per cent of the total males operated on) as against thirty-one females (17 per cent of the total females operated on).

Causes of death in the eighty-two cases with available data were thirty-one due to cerebrovascular accident, twenty-nine to cardiac failure, twenty-one to renal failure and five to causes other than hypertension. (Note: The discrepancy in the total number of cases is due to the fact that four cases were diagnosed as "cardiorenal failure" and hence were included in both categories.)

SUMMARY

Three hundred and fifty consecutive cases of hypertension with operation by bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy have been studied over a period of nearly seven years.

From table 33 it must be concluded that the operation of bilateral supradiaphragmatic splanchnicectomy

TABLE 33.—*Summary of Results of Splanchnicectomy: Percentage of Cases Studied Showing Improvement (From Nine Months to Seven Years After Operation) **

	Per Cent
Blood pressure	11.7
Reduced to normal.....	7.6
Markedly reduced (but not to normal).....	51.4
Total cases significantly reduced.....	59.0
General disability	86.6
Symptoms improved	55.5
Complete recovery incapacitation.....	81.3
Total cases with improvement incapacitation.....	81.3
Eye grounds	73.5
Disappearance of papilledema, when present.....	69.4
Total cases with improvement.....	69.4
Heart	64
Heart size diminished.....	51.4
Electrocardiogram improved	51.4
Renal function	52.2
Urea clearance improved.....	41.8
Urine concentration improved.....	41.8

* Statistics include those patients who showed improvement but who subsequently died.

and lower dorsal sympathetic ganglionectomy is of great value in the treatment of hypertension.

Of the patients studied 86.6 per cent had postoperative relief of major symptoms, especially headache, 81.3

per cent had improvement or complete relief of incapacitation and 51.4 per cent with adequate postoperative data had a significant reduction in blood pressure. Approximately one half of these patients had pressures reduced to normal or markedly reduced.

Improvement in ophthalmologic, cardiac and renal status following operation varied from 45 per cent to 70 per cent of the cases studied.

Prognosis is much more favorable in females than in males.

The most favorable results are obtained in the age group before 30. Following this period the age of the patient appears to be of minor importance as far as the result of operation is concerned.

Far advanced fundus changes, i. e. marked angiospasm and papilledema, are not contraindications to the operation.

The operative mortality is low (3.4 per cent) and no specific ill effects are attendant on the operation.

Finally, no other form of therapy, whether medical or surgical, has as yet been reported which offers as good results in patients suffering from hypertension of an equal degree of severity. Furthermore, these results are not temporary but continue over a period of years.

The conclusion is reached that the surgical treatment of hypertension by bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy offers a better prognosis in cases of severe hypertension than any other form of therapy as yet reported.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

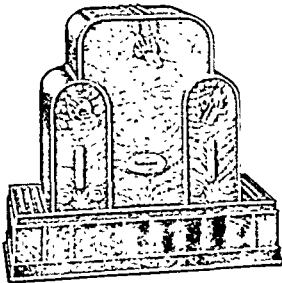
"TWIN CONTROL" HEAVY DUTY CAUTERY SET, "SINGLE CONTROL" CAUTERY SET AND "SIMPLIFIED CONTROL" CAUTERY SET ACCEPTABLE

Manufacturer: National Electric Instrument Company, Inc., 36-06 Forty-Second Avenue, Long Island City, N. Y.

The Cautery Sets submitted by the National Electric Instrument Company, Inc., consist of the following: "Single Control" Cautery Set designed to operate the lighter cautery tips manufactured by the firm (Nos. 1 to 7) and two larger units, the "Twin Control" Heavy Duty Cautery Set and the "Simplified Control" Cautery Set, designed to operate the heavier tips as well as the lighter ones.

According to information supplied by the firm, the heating elements of the cautery electrodes are made of "Nichrome" and are silver soldered into the shanks. Molded shank separators provide for insulation and rigidity.

The cautery pistol is molded of a boilable material known as "Neicomold" and a button momentary type of control switch, as well as a trigger lock for more lengthy cautery procedures. All internal contacts are of phosphor bronze and copper. The rubber-covered cautery pistol conductor cable is composed of two conductors of No. 13 copper, made up of 120 strands of No. 34 copper wire.



"Simplified Control" Cautery Set.

The transformers are of split primary windings. This construction is said to result in more efficient heat dissipation. The molded transformer housings provide efficient insulation and each of the terminals of the metal transformer is insulated from the metal panels by means of fiber or bakelite washers and bushings.

The Council's clinical investigation of the apparatus revealed that it gave satisfactory service. The cautery blades, which are of several sizes, can be heated from a dull red to almost white heat and retain this heat well when applied to the tissues; they do not cool down too rapidly to be effective. For cauterization within cavities, the instrument is accompanied by a light which is regulated from the instrument box itself.

The following results were obtained from physical tests performed in the Council's laboratory.

The "Twin Control" Heavy Duty Cautery Set was run for one hour, a No. 9 electrode and cautery light being used as load. The electrode was immersed in water to keep it from melting. The final temperature by the thermometer method was 95 C. and by the resistance method was 91.7 C. The input was 110 volts and 15 watts.

The "Single Control" Cautery Set was run for one-half hour, a No. 2 electrode immersed in water being used as a load. The final temperature by the thermometer method was 105 C. and by the resistance method 91.7 C. The input was 110 volts and 10 watts.

The Council voted to accept the "Twin Control" Heavy Duty Cautery Set, the "Single Control" Cautery Set and the "Simplified Control" Cautery Set for inclusion on its list of accepted devices.

MONTGOMERY WARD S-1 SUNLAMP ACCEPTABLE

Distributor: Montgomery Ward & Co., Chicago.

The Montgomery Ward S-1 Sunlamp, manufactured by the General Electric Company, produces ultraviolet radiation within the limits of the standards set by the Council for devices using the term "Sunlamp," which require that the energy of wavelengths shorter than and including 2,800 angstroms shall not exceed 1 per cent of the total energy of wavelengths between 2,804 and 3,132 angstroms. The wavelengths fall in the spectral region of low erythematogenic action and render the sunlamp suitable for unsupervised use by the layman.

The Mazda Sunlight Lamp Type S-1 is mounted in a reflector on an adjustable support and is a combination of tungsten electrodes in parallel with a tungsten filament. These are enclosed in a special glass bulb along with a little pool of mercury. The current first flows only through the filament but, as the temperature increases, the mercury vaporizes and an arc is formed between the ends of the tungsten electrodes. The process requires only a few seconds, although a few minutes is required for the lamp to begin radiating ultraviolet energy at its maximum efficiency. The mercury arc between the electrodes produces the major portion of the effective ultraviolet radiation. The result of the combination produces radiations in the visible and the infra-red as well as in the ultraviolet zones. The bulb is made of Pyrex glass, which absorbs most of the radiation in the ultraviolet region shorter than approximately 2,800 angstrom units.

The lamp operates only on alternating current; type S-1 requires an input of 450 watts. The lamp stands are equipped with special transformers in the base for the purpose of securing the proper voltage, since the S-1 bulbs do not fit in the ordinary lamp socket.

The Montgomery Ward S-1 Sunlamp generates 50 micro-watts per square centimeter at a distance of 45 inches from the rim of the reflector. A minimum perceptible erythema may be produced at a distance of 45 inches in twenty minutes on the average untanned skin.

The Council voted to accept the Montgomery Ward S-1 Sunlamp for inclusion on its list of accepted devices.



Montgomery Ward S-1 Sunlamp.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING STATEMENT.

PAUL NICHOLAS LEECH, Secretary.

PURIFIED PROTEIN DERIVATIVE OF TUBERCULIN

Action on Name

Dr. Esmond R. Long inquired of the Council some time ago whether or not the name Purified Protein Derivative would be acceptable to the Council on Pharmacy and Chemistry as a designation for the purified protein principle of tuberculin. The Council voted that it would recognize the name Purified Protein Derivative of Tuberculin with the understanding that the initials P. P. D., which are widely used colloquially, will not be used in official designation of the product, as on packages or circulars.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

AMINOPHYLLINE (See New and Nonofficial Remedies, 1940, p. 555).

The following dosage forms have been accepted:

Tablets Aminophylline, 0.1 Gm. (1½ grains).

Prepared by Endo Products, Inc., Richmond Hill, N. Y.

Ampule Solution Aminophylline, 0.48 Gm., 2 cc.

Prepared by Endo Products, Inc., Richmond Hill, N. Y.

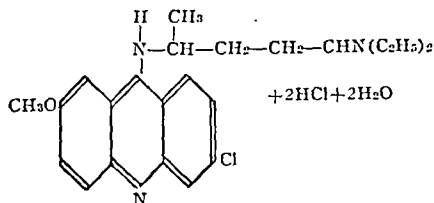
Ampule Solution Aminophylline, 0.24 Gm., 10 cc.

Prepared by Endo Products, Inc., Richmond Hill, N. Y.

Tablets Aminophyllin 0.1 Gm. (1½ grains).

Prepared by The Smith-Dorsey Company, Lincoln, Neb.

ATABRINE di-HYDROCHLORIDE.—Chinacrin Dihydrochloride.—The di-hydrochloride of 3-chloro-7-methoxy-9-(1-methyl-4-diethyl-amino)butylamino acridine.—



Actions and Uses.—Atabrine di-hydrochloride destroys the asexual forms of *Plasmodium vivax* and *P. malariae*, but the crescents of *P. falciparum* are more resistant. It does not induce hemolysis or cause damage to the liver or circulatory system when used therapeutically. It may cause epigastric distress and cramps, but it is of low toxicity when administered orally. The spleen of chronic malaria is not affected by atabrine di-hydrochloride but the acutely enlarged spleen yields, though more slowly, than to quinine. Its relative antimalarial value compared to that of quinine is much debated. It is claimed to act more rapidly and to require a shorter period of treatment. It does not induce symptoms of cinchonism, and it may be used during pregnancy. Its prophylactic value appears to be about equal to that of quinine. It is absorbed readily from the intestine and is excreted slowly in the urine and feces. While it is sometimes injected intramuscularly or even intravenously in cases of severe malarial infection when oral administration is not feasible, the intravenous injection is dangerous; the injections must be made very slowly. (See report of Field, J. W.; Niven, J. C., and Hodgkin, E. P.: Prevention of Malaria in Field by Use of Quinine and Atebrin (Atabrine); Experiments in Clinical Prophylaxis, Bull. Health Organ., League of Nations 6:236 [April] 1937.)

Dosage.—Oral. Adults: 0.1 Gm. (1½ grains) three times daily for five days. Children of 1 to 4 years: 0.05 Gm. (¾

grain) twice daily for five days or once daily for eight days, crushed and suspended in honey or syrup. Children of 4 to 8 years: 0.1 Gm. (1½ grains) twice daily for five days or once daily for eight days. Children over 8 years: Dosage like that of adults.

Prophylactic Dose: Adults: 0.2 Gm. (3 grains) twice weekly, or 0.05 Gm. (¾ grain) daily. Children: 0.05 Gm. (¾ grain) every other day.

The technic of the intramuscular or intravenous administration must be learned before the method is used. Details will be found in the circulars of manufacturers and in various publications.

Manufactured by the Winthrop Chemical Company, Inc., New York. U. S. patent 2,113,357 (April 5, 1938; expires 1955). U. S. trademark 302,473.

Ampules Atabrine di-Hydrochloride Powder 0.2 Gm. with Ampules, 10 cc. size, Sterile Distilled Water.

Tablets Atabrine di-Hydrochloride (Sugar Coated) 0.1 Gm. (1½ grains).

Tablets Atabrine di-Hydrochloride 0.1 Gm. (1½ grains).

Tablets Atabrine di-Hydrochloride 0.05 Gm. (¾ grain).

Atabrine di-hydrochloride occurs as an odorless, orange-yellow, bitter tasting, crystalline powder, containing two molecules of water of crystallization; it melts with decomposition between 245 and 247°C. It is soluble in water and slightly soluble in acetone, ether and benzene. Aqueous solutions of atabrine di-hydrochloride are colored yellow and exhibit yellow-green fluorescence.

Dissolve about 25 mg. of atabrine di-hydrochloride in 2 cc. of sulfuric acid, cover the yellow solution obtained with 0.5 cc. of nitric acid; a dark red color develops in the zone of contact and, on shaking, the solution turns red with loss of fluorescence.

Dissolve 1 Gm. of atabrine di-hydrochloride in 50 cc. of water. To a 5 cc. portion add 1 cc. of dilute ammonia water; an oily, yellow precipitate results. Add 5 cc. of amyl alcohol to the mixture and shake the test tube; the amyl alcohol layer contains the free base, atabrine.

To the first of four separate 5 cc. portions of the solution add 1 cc. of mercury bichloride solution; to the second portion add 1 cc. of potassium iodide solution; to the third portion add 1 cc. of ammonium thiocyanate solution; and to the fourth portion add 1 cc. of potassium dichromate solution; a yellow precipitate is produced in each mixture. To another 5 cc. portion add 2 drops of nitric acid and 5 drops of silver nitrate solution; a white precipitate forms, soluble in excess ammonia water. To another 5 cc. portion add 1 cc. of barium chloride solution; no turbidity results.

The *pn* of a solution made by dissolving 1 Gm. of atabrine di-hydrochloride, accurately weighed, in boiled and cooled distilled water sufficient to make 100 cc. of solution is between 4.5 and 4.9 at 25°C.

Dry about 1 Gm. of atabrine di-hydrochloride, accurately weighed, to constant weight at 100°C.: the loss in weight should not be less than 5.5 per cent nor more than 7.5 per cent.

Incinerate 1 Gm. of atabrine di-hydrochloride; the ash is negligible.

Transfer 1 Gm. of atabrine di-hydrochloride, accurately weighed, to a 100 cc. calibrated flask and add 50 cc. of water. When the salt has dissolved, add slowly 4.5 cc. of normal sodium hydroxide solution, mix with swirling (avoid air bubble entrapment) and fill to the mark with water. Filter the solution into a dry 250 cc. beaker, and add about 0.3 Gm. of halogen-free decolorizing charcoal. Stir the mixture and allow it to stand for five minutes; then filter through a dry paper. Reject the first 25 cc. of the colorless filtrate, take 50 cc. of the remainder, and titrate as directed under volumetric method 1 in Official and Tentative Methods of Analysis of the Official Agricultural Chemists, edition 4, 1935, page 131. The calculated content of hydrochloric acid should not be less than 14.1 per cent nor more than 14.6 per cent.

Transfer about 0.25 Gm. of atabrine di-hydrochloride, accurately weighed, to a 100 cc. calibrated flask, add 10 cc. of water and 26 cc. of a solution made by dissolving 26 Gm. of sodium acetate and 26 cc. of 40 per cent acetic acid in sufficient water to make a total of 100 cc. To the solution in the calibrated flask add 50 cc. of tenth-normal potassium dichromate and water to the mark. Avoid air bubble entrapment. Mix thoroughly and filter the solution through a dry paper, rejecting the first 15 cc. of the filtrate. Transfer 50 cc. of the filtrate to a glass-stoppered Erlenmeyer flask, add 13 cc. of hydrochloric acid and 20 cc. of potassium iodide test solution. Stopper the flask and mix the contents by swirling gently. Allow the mixture to stand in the dark for two minutes and titrate the liberated iodine with tenth-normal sodium thiosulfate. Each cubic centimeter of tenth-normal potassium dichromate used is equivalent to 0.007881 Gm. of anhydrous atabrine di-hydrochloride. Add 3 mg. to the weight found to compensate for inherent errors of the method. The content of anhydrous atabrine di-hydrochloride should be not less than 92.5 per cent or more than 94.5 per cent.

PROCAINE HYDROCHLORIDE-ABBOTT (See New and Nonofficial Remedies, 1940, p. 81).

The following additional dosage forms have been accepted:

Ampoules Procaine Hydrochloride 1%, W/V, 1½ cc.: Each 1½ cc. contains procaine hydrochloride-U. S. P. 0.015 Gm., sodium chloride and chemically pure water to make an isotonic solution.

Ampoules Procaine Hydrochloride 1%-Epinephrine 1:50,000 Solution, 2 cc.: Each 2 cc. contains procaine hydrochloride-U. S. P. 0.02 Gm. (½ grain), epinephrine 0.00004 Gm. (¼,600 grain) and sodium bisulfite 0.002 Gm. in isotonic solution.

BOVINE TETANUS ANTITOXIN (See New and Nonofficial Remedies, 1940, p. 419).

Mulford Biological Laboratories, Sharp & Dohme, Philadelphia.

"Lyovac" Tetanus Antitoxin (Bovine).—An antitoxin derived from the blood serum of cattle immunized against the toxin of *Bacillus tetani* (Clostridium tetani). It is packaged by the "Lyovac" process, which consists essentially of rapid freezing at a temperature far below the freezing point, together with rapid dehydration under high vacuum without

melting or fusing of the original frozen substance. Marketed in packages containing one ampule vial of lyophilized antitoxin representing 1,500 units and a 3 cc. ampule vial containing distilled water for restoration of the antitoxin, with a 1 cc. ampule vial of normal bovine serum (1:10 dilution) for sensitivity tests; and in packages containing one ampule vial of lyophilized antitoxin representing 10,000 units and a 20 cc. ampule vial containing distilled water for restoration of the antitoxin, with a 1 cc. ampule vial of normal bovine serum (1:10 dilution) for sensitivity tests.

PHYSIOLOGICAL SOLUTION OF SODIUM CHLORIDE (See New and Nonofficial Remedies, 1940, p. 379).

The following dosage form has been accepted:

Ampoule Physiological Solution of Sodium Chloride, 50 cc.
Prepared by Endo Products, Inc., Richmond Hill, N. Y.

SODIUM MORRHUATE (See New and Nonofficial Remedies, 1940, p. 486).

The following dosage forms have been accepted:

Ampoule Solution Sodium Morrhuate 5% with Benzyl Alcohol 2%, 2 cc.: Each cubic centimeter contains sodium morrhuate 0.05 Gm. and benzyl alcohol 0.02 Gm. in aqueous solution.

Prepared by Endo Products, Inc., Richmond Hill, N. Y. No U. S. patent or trademark.

Ampoule Solution Sodium Morrhuate 5% with Benzyl Alcohol 2%, 5 cc.: Each cubic centimeter contains sodium morrhuate 0.05 Gm. and benzyl alcohol 0.02 Gm. in aqueous solution.

Prepared by Endo Products, Inc., Richmond Hill, N. Y. No U. S. patent or trademark.

Solution Sodium Morrhuate 5% with Benzyl Alcohol 2%, 25 cc. Bottle: Each cubic centimeter contains sodium morrhuate 0.05 Gm. and benzyl alcohol 0.02 Gm. in aqueous solution.

Prepared by Endo Products, Inc., Richmond Hill, N. Y. No U. S. patent or trademark.

ASCORBIC ACID (See New and Nonofficial Remedies, 1940, p. 530).

The following dosage forms have been accepted:

Tablets Ascorbic Acid, 15 mg.

Prepared by the Upjohn Company, Kalamazoo, Mich.

Tablets Ascorbic Acid, 25 mg.

Prepared by the Upjohn Company, Kalamazoo, Mich.

Tablets Ascorbic Acid, 50 mg.

Prepared by the Upjohn Company, Kalamazoo, Mich.

Tablets Ascorbic Acid, 100 mg.

Prepared by the Upjohn Company, Kalamazoo, Mich.

NICOTINIC ACID (See New and Nonofficial Remedies, 1940, p. 524).

The following dosage forms have been accepted:

Tablets Nicotinic Acid, 20 mg.

Prepared by the Upjohn Company, Kalamazoo, Mich.

Tablets Nicotinic Acid, 50 mg.

Prepared by the Upjohn Company, Kalamazoo, Mich.

Tablets Nicotinic Acid, 100 mg.

Prepared by the Upjohn Company, Kalamazoo, Mich.

MERCURIC SUCCINIMIDE (See New and Nonofficial Remedies, 1940, p. 338).

Endo Products, Inc., Richmond Hill, N. Y.

Ampoules Mercury Succinimide-Endo, 0.01 Gm. (1/10 grain), 1 cc.

SODIUM THIOSULFATE (See New and Nonofficial Remedies, 1940, p. 488).

The following dosage forms have been accepted:

Ampoules Sodium Thiosulfate Solution-Endo, 0.5 Gm., 5 cc.

Prepared by Endo Products, Inc., Richmond Hill, N. Y.

Ampoules Sodium Thiosulfate Solution-Endo, 1.0 Gm., 10 cc.

Prepared by Endo Products, Inc., Richmond Hill, N. Y.

SULFANILAMIDE (See New and Nonofficial Remedies, 1940, p. 489).

The following dosage forms have been accepted:

Tablets Sulfanilamide-Endo, 5 grains.

Prepared by Endo Products, Inc., Richmond Hill, N. Y. No U. S. patent or trademark.

Tablets Sulfanilamide-Endo, 7 1/2 grains.

Prepared by Endo Products, Inc., Richmond Hill, N. Y. No U. S. patent or trademark.

QUINIDINE SULFATE (See New and Nonofficial Remedies, 1940, p. 395).

The following dosage form has been accepted:

Capsules Quinidine Sulfate, 0.2 Gm. (3 grains).

Prepared by the Abbott Laboratories, North Chicago, Ill.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING ADDITIONAL FOODS HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO ACCEPTED FOODS.

FRANKLIN C. BING, Secretary.

Yeast of High Vitamin B₁ Content for Bakers

The Council has encouraged the restorative addition of essential vitamins and minerals to processed foods as one method of facilitating the selection of a diet that is adequate for good health. A pound loaf of ordinary white bread provides about 50 to 100 international units of vitamin B₁. A pound loaf of whole wheat bread (meaning the genuine whole wheat bread) provides about 450 international units of vitamin B₁. The thiamine content of white bread may be increased in a variety of ways. One method consists in the use of high vitamin B₁ potency yeast in place of the ordinary yeast that is used for leavening the dough.

The following product has been given consideration by the Council and found acceptable as a preparation for increasing the nutritive value of ordinary bread with respect to vitamin B₁:

FOODS FOR SPECIAL DIETETIC PURPOSES (See Accepted Foods, 1939, p. 295).

Standard Brands Incorporated, New York.

FLEISCHMANN'S HI-B YEAST FOR BAKERS, a variety of baker's yeast, *Saccharomyces cerevisiae*, cultured to yield a product of high vitamin B₁ content. The yeast is distributed in compressed cakes, weighing 1 pound and containing 30,000 international units of vitamin B₁, for use by bakers as an ingredient of bread doughs. Before shipment every batch of yeast is tested for vitamin content and baking strength and also is examined bacteriologically.

Analysis (submitted by manufacturer).—Moisture 70.0%, total solids 30.0%, ash 1.8%, fat (ether extract) 0.5%, protein (N \times 6.25) 15.5%, glycogen 9.5%, yeast fiber 2.7%, carbohydrates other than yeast fiber (by difference) 9.5%.

Assays show that the product uniformly contains not less than 30,000 international units of vitamin B₁ to the pound. Other vitamins of the B complex natural to yeast also are present. Used in the amount of 2 per cent in a bread formula (2 pounds of compressed yeast to 100 pounds of flour) the resulting bread contains approximately 450 international units of vitamin B₁ to the pound loaf.

PREPARATIONS USED IN THE FEEDING OF INFANTS (See Accepted Foods, 1939, p. 156).

Gerber Products Co., Fremont, Mich.

GERBER BRAND STRAINED PEAR AND PINEAPPLE.

Analysis (submitted by manufacturer).—Moisture 81.5%, total solids 18.5%, ash 0.3%, protein (N \times 6.25) 0.3%, fats (ether extract) 0.3%, crude fiber 0.7%, carbohydrates other than crude fiber (by difference) 16.9%, calcium¹ (Ca) 0.0096%, phosphorus (P) 0.0078%, iron (Fe) 0.0019%.²

Calories.—0.72 per gram; 20.4 per ounce.

H. J. Heinz Company, Pittsburgh.

HEINZ BRAND STRAINED TOMATO SOUP, a canned condensed strained cooked mixture of tomatoes, carrots, potatoes, celery, sucrose, rice, soy bean flour, dried whey and sodium chloride.

Analysis (submitted by manufacturer).—Moisture 83.7%, total solids 16.3%, ash 1.3%, sodium chloride (NaCl) 0.8%, fat (ether extract) 0.1%, protein (N \times 6.25) 2.0%, crude fiber 1.6%, carbohydrates other than crude fiber (by difference) 10.8%, total sugar 9.4%, calcium (Ca) 0.0221%, phosphorus (P) 0.039%, iron (Fe) 0.0009%, copper (Cu) 0.00021%, acidity as citric acid 0.49%, pH 4.4.

Protocols of biologic assay submitted by manufacturer (1940) showed that this product contains 23.17 international units of vitamin A, 0.262 international unit of vitamin B₁, and 0.505 Sherman-Hourquin unit of riboflavin per gram; 656.8, 7.4 and 14.3 per ounce. Report of chemical titration (1940) showed that the product contained 5.4 international units of vitamin C per gram, 153 per ounce.

Calories.—0.54 per gram; 15 per ounce.

UNCLASSIFIED AND MISCELLANEOUS FOODS, PEANUT BUTTER (See Accepted Foods, 1939, p. 381).

Rose Field Packing Company, Ltd., Alameda, Calif.

SKIIPPY BRAND PEANUT BUTTER CHUNK STYLE, regular peanut butter to which one-eighth inch particles of roasted peanuts have been added, sugar and sodium chloride.

Analysis (submitted by manufacturer).—Moisture 0.4%, total solids 99.6%, ash 3.1%, fat (ether extract) 49.1%, protein (N \times 6.25) 30.8%, crude fiber 0.9%, carbohydrates other than crude fiber (by difference) 11.3%.

Calories.—6.3 per gram; 179 per ounce.

1. Calcium was determined by the method of Meloche, W. V.; Clifcorn, L. E., and Griem, W. B.: Determination of Calcium in Mineral Mixtures. J. A. O. A. C. 18: 240 (May) 1935.

2. Iron determined by the method of Winsor, H. W.: Intensity and Stability of Ferric Thiocyanate Color, Ind. Eng. Chem., Analytical Ed. 9: 453, 1937.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 30, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

FULL TIME TEACHING IN CLINICAL MEDICINE

In 1900 there were some 155 medical colleges in the United States. Today the number of four year medical schools is sixty-six. In those days medical schools included some for which preparation was merely high school graduation, a few which required some university education. Today the majority of medical students have had at least three years of college education before entering on the study of medicine. Thus has come about a tremendous advancement of standards. No doubt the first great impetus toward that advancement came when the American Medical Association established the Council on Medical Education and Hospitals and began publishing regularly the statistics on medical schools and on licensing boards. However, the situation was dramatized when the first report by Abraham Flexner was published under the auspices of the Carnegie Foundation for the Advancement of Teaching. This publication served to call public attention to the neces-

sity for improvement and thereby gave to the American Medical Association the type of support that it needed in its drive for educational advancement. The work here mentioned is probably the best known contribution of Abraham Flexner. However, his autobiography, recently published,¹ serves to remind us of many other valuable contributions to the civilization of our times.

At the age of 17 Abraham Flexner was sent to Johns Hopkins University. It becomes obvious, as one follows through Mr. Flexner's career, that Johns Hopkins and what he saw later in Germany influenced him tremendously and through him came to have a significant effect on all American medical education. He developed the concept that German medical education was sound precisely where American medical education was deficient, referring particularly to adequate entrance requirements which were enforced, close relationships between the laboratories and clinics, teachers who were professors and not practicing physicians, and a high place for research. He found some minor defects in German medical education but he does not emphasize these greatly.

If there is any one aspect of Mr. Flexner's recommendations that has agitated American medicine in recent years, it is the question of full-time versus part-time clinical teaching. In his twelfth chapter Mr. Flexner tells the story of the introduction of the full-time system. According to Mr. Flexner, he himself is not to be credited with the authorship of what is called the full-time scheme. He relates that the suggestion came to him from Dr. Mall, eminent professor of embryology and anatomy in Johns Hopkins University Medical School, when Dr. Mall said "If the school could get a sum of approximately a million dollars, in my judgment there is only one thing that we ought to do with it—use every penny of its income for the purpose of placing upon a salary basis the heads and assistants in the leading clinical departments, doing for them what the school did for the underlying medical sciences when it was started." The scheme, however, did not originate with Dr. Mall but is attributed to the great Leipzig physiologist Ludwig, who one day, so Mall said, remarked to him that sooner or later teaching and research in clinical medicine and surgery would have to be organized on the same basis as teaching and research in anatomy and pathology. It is asserted that both of these had once been in the hands of practicing physicians and neither had prospered as they should until they commanded the full time and strength of the men engaged in their teaching and cultivation. Mr. Flexner reports that this scheme was unanimously endorsed by the laboratory men but there was a rift among the clinicians, and that the opinion of Dr. William Osler, then at Oxford, was adverse. Since the establishment of the full-time plan it has been a constant subject of debate among medical educators. In the United States today our medical schools vary from

1. Flexner, Abraham: I Remember, New York, Simon and Schuster, 1940.

some which have a majority of full-time teachers in the clinical branches to one of our leading medical schools which still has none. No doubt an impartial evaluation of our educational system would recognize certain aspects of full-time teaching which are desirable but would also recognize some of the defects which the introduction of this system has created.

One of the extraordinary phenomena of the entrance of the full-time teacher into medical education has been a sort of group attitude in questions concerning medical economics. Here is perhaps a problem to which the sociologist or psychologist might well give special attention. In questions concerning the costs and distribution of medical service, in problems of political and governmental character that have agitated the medical profession in recent years, there has failed to be a community of interest. Part or full-time teachers in the medical schools have not in general supported the elected representatives of the medical profession. True, there have been on both sides individuals who have departed from the herd. In general, the alignments have been as here suggested.

As the leaders of one group have sought for federal funds to aid the medical schools, practitioners of medicine have asserted that they were concerned primarily with their own rather than with the public good. As the practitioners of medicine have sought to maintain independence from governmental control, the teaching groups have charged that they were protecting their professional interest in the patient's pocketbook and have not been concerned with the public good. Obviously the economic situation of the schools, and of the private practitioners as well, in these times of stress has brought about extraordinary conditions in which the true issues may occasionally have been lost to sight. The problem of educating physicians for the care of the sick and the increasing costs of medical education, associated with university control, may have some responsibility for this situation.

Incidentally, the answer to the problem of medical care cannot lie in state provision of medical care to be given under the auspices of medical educational institutions. The mere fact that there exist so many states in which there are institutions for medical education, that there are such wide areas in which educational institutions are not available, the fact that educational institutions tend to multiply in large centers where a mass of so-called clinical material is available for teaching purposes, would indicate that the chief purpose of the educational institution is to educate and that the chief purpose of the physician is the care of the sick.

Unfortunately the assumption of these attitudes seems to result in a loss of interest by the practicing medical profession in the whole problem of medical education. The physicians of large cities have become interested because there is obviously a social, professional and educational advantage in being associated with a teaching institution. Physicians far removed,

however, from teaching centers express disinterest in many instances simply because they have felt that the teaching institutions were much more concerned with their own prestige and advancement than with the primary problems of medical practice. The extension of the functions of medical education to the field of graduate education of the practicing physician would unquestionably bring these physicians again within the fold of medical education.

MECHANISM OF EXPERIMENTAL RENAL HYPERTENSION

From a study of the hemodynamics of the perfused isolated canine kidney, Kohlstaedt and Page¹ of the Lilly Laboratory for Clinical Research, Indianapolis, have formulated a definite theory as to the method of production of arterial hypertension, subsequent to experimental renal ischemia.

Six years ago Goldblatt and his co-workers² of the Institute of Pathology, Western Reserve University, proved that in dogs renal ischemia caused by bilateral compression of the renal arteries is almost invariably followed by a definite and persistent elevation in systolic blood pressure. Since this secondary hypertension is not prevented by preliminary denervation to the kidneys, it seemed logical to assume that it is due to some unknown retention product or internal secretion from the kidneys. Transplantation of ischemic kidneys into normal dogs confirmed the so-called internal secretion theory. Much experimental and clinical evidence seems to indicate that renin may be the pathologic internal secretion responsible for this hypertension, even though it has not been shown to the satisfaction of most clinicians that renin is actually liberated by the ischemic kidney. Proof is made difficult by the fact that renin in itself is not a pressor substance and requires chemical activation to produce vasoconstriction.

In order to confirm the renin hypothesis, Kohlstaedt and Page perfused the isolated normal canine kidney with defibrinated blood under varying hemodynamic conditions. Venous blood samples drawn from these perfused kidneys were activated with renin complement and the resulting angiotonin titrated for pressor effects by pulsate perfusion through the isolated rabbit ear.

Excised normal canine kidney perfused under normal pulsate arterial pressure did not secrete renin into the venous blood. Venous blood collected at the beginning and the end of such perfusions showed no differences in vasoconstriction properties when complemented with renin activator. When the renal artery was partially clamped, however, and the resulting reduced blood flow continued for 100 or more minutes, the venous blood samples acquired vasoconstrictor properties. Renin secretion was not prevented by increasing the rate of perfusion flow to normal by increasing the per-

1. Kohlstaedt, K. G., and Page, I. H.: *J. Exper. Med.* 72:201 (Aug.) 1940.

2. Goldblatt, Harry; Lynch, James; Hanzal, R. F., and Summerville, W. W.: *J. Exper. Med.* 59:347 (March) 1934.

fusion pressure. From this and from other hemodynamic tests the authors conclude that the essential cause of renin liberation is not changes in blood pressure or perfusion rate but reduced pulse pressure. Numerous investigators have shown that perfusion of isolated organs under constant pressure almost invariably leads to edema, a pulsate perfusion being necessary for normal tissue maintenance. Presumably a pulsate pressure is necessary for adequate interstitial lymph drainage.

Summarizing their experimental evidence, the Indianapolis clinicians formulate a definite theory. According to this theory, compression of the renal artery "leads to partial conversion of pulsate to continuous blood flow in the kidney with edema and anoxia of the cells of the tubules as the chief results. Increase in cellular membrane permeability follows and allows the liberation of the large renin molecule. Renin reacts with renin activator to produce angiotonin, which itself raises blood pressure and causes efferent glomerulin arteriolar constriction and further tubular anoxia. A vicious circle may be thus set up which results in sustained arterial hypertension."

While this pulse pressure theory will require experimental and clinical confirmation before it can be definitely accepted, it would seem to be the only definite theory thus far suggested to explain the physiologic mechanism of experimental renal hypertension. It is a provocative working hypothesis for further clinical research. The possible antigenic properties of homologous renin and angiotonin are now under investigation.

Current Comment

MR. MACFADDEN DISCUSSES ARMY MEDICAL SERVICE

In the current issue of *Liberty* Mr. Bernarr Macfadden, its publisher, signs an editorial in which he proposes that homeopaths, osteopaths, naturopaths and chiropractors be given a chance to demonstrate the value of their methods, using the soldiers of the American army as guinea pigs. He cites statistics to indicate that osteopaths lost only one fourth of 1 per cent of their patients from influenza in the 1918 epidemic and that doctors lost from 5 to 6 per cent. He says that osteopaths had a fatality record of 10 per cent for pneumonia as compared with a medical fatality record of 33 per cent. As for the chiropractors, Mr. Macfadden indicates that they claim even better records. Obviously the validity of such statistics is highly questionable, even taking into account the fact that anybody who gets sick enough gets a doctor and that therefore mortality rates would naturally be higher for the seriously sick than for people who are not seriously sick. Furthermore, there would also be a considerable amount of doubt as to the diagnoses made by incompletely and peculiarly trained cultists as contrasted with the scientific diagnoses made by physicians. People who diagnose in their patients diseases which do not exist find it easy to cure such cases. When a common cold is called influenza and

pneumonia, it is easy to claim a cure. Many a cold gets well without any treatment whatever. Mr. Macfadden complains, incidentally, that the soldiers overeat and that their work is not sufficient to take up their food intake. This generalization is made, of course, without the slightest knowledge on his part of just how much soldiers eat or of the considerable scientific attention that is being given to nutrition for American soldiers. Fortunately for the American soldier the medical corps is under the direction of competent officials, and the work of that department is, in turn, controlled by the general staff. No doubt these men realize their obligation to the young men who are under their care and will not permit themselves to be swayed by the extravagant claims of irresponsible cultists or by the distorted diatribes of Bernarr Macfadden.

ALCOHOL AND THIAMINE IN NUTRITION

The amount of food consumed by those who regularly drink alcohol in considerable quantities influences the development of the so-called alcoholic diseases. Once a full diet was thought to counteract toxic effects of alcohol, but now it is known that certain of these typical diseases—Korsakoff psychosis, alcoholic polyneuritis, pseudopellagra and some types of encephalopathia alcoholica—are real vitamin deficiencies. Fantus¹ has recently emphasized various obvious as well as more subtle factors influencing the thiamine intake; inadequate consumption of foods containing vitamin B₁ is plainly of importance and the statement is made that "chronic alcoholism is the most frequent predisposing factor in cases of severe involvement in Cook County Hospital," which situation is undoubtedly typical of other large centers. According to Jolliffe,² alcohol may contribute to nutritional deficiency disease by decreasing appetite as a result of its irritant action on the gastrointestinal mucosa, by interference with absorption, by substituting its "vitamin-free" calories for energy in the form of vitamin-containing food and by disturbing the ratio between metabolizable energy and thiamine. Only when the vitamin/calory ratio is maintained above a marginal value will there be freedom from subclinical or outspoken signs of deficiency; a diet can be rendered inadequate by either decreasing the vitamin intake or increasing the vitamin-free sources of calories. Jolliffe has shown that the rather narrow margin of safety in the modern American dietary with respect to adequacy of vitamin B₁ can be greatly decreased or largely erased by the consumption of alcohol, since the metabolism of the alcohol calories increases the need for thiamine which the alcohol itself cannot provide. Frequently the true etiology of the vitamin deficiency disease is obscured by naming the disease after the condition responsible for the increased demand for the vitamin as, for instance, "diabetic," "metabolic," "infectious," "gestational" or "gastrogenous" polyneuritis. Obviously a close relationship exists between energy metabolism and thiamine requirement.

1. Fantus, Bernard; Traut, E. F., and Greenebaum, Regina S.: The Therapy of Subvitaminosis B₁, J. A. M. A. 115: 450 (Aug. 10) 1940.
2. Jolliffe, Norman: The Influence of Alcohol on the Adequacy of the B Vitamins in the American Diet, Quart. J. Studies on Alcohol 1: 74 (June) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

NEW ARMY HOSPITALS

New army hospitals are to be built in New Orleans, Savannah, Ga., and Hinesville, Ga., under the defense appropriation bill, according to *Modern Hospital*. The \$1,200,000 cantonment hospital planned for New Orleans will have a capacity of 1,000 beds and will be of the pavilion type, probably of temporary construction. It will be located in the New Orleans lake shore development along Lake Pontchartrain, according to present plans, and will be used to give treatment to men stationed at Camp Beauregard and other army establishments in that section of the country.

A hospital of from 150 to 200 beds has been approved for the airport in Savannah to provide for the 3,500 officers and men of the air corps stationed there. For the Savannah anti-aircraft area with six regiments, or about 15,000 men, an institution of from 600 to 800 beds will be constructed at Hinesville. The hospitals to be built in Georgia are expected to be replaced later by more substantial structures, since the Savannah and Savannah area army bases will be permanent.

CONFERENCE OF CORPS AREA SURGEONS

A meeting of corps area surgeons was held at the office of the surgeon general, U. S. Army, Washington, D. C., October 14-16, to discuss problems arising from the induction of the National Guard, expansion of the Army and induction of trainees. Major Gen. James C. Magee, surgeon general, presided. All corps area surgeons, except Col. Will L. Pyles of the Fifth Corps Area, as well as heads of divisions in the office of the surgeon general were present. Among other matters, it was decided to station a nurse at headquarters of each corps area to advise the corps area surgeon on matters affecting nurses, especially in connection with the procurement of 4,019 nurses within the next few months for active duty with the Army.

NATIONAL DEFENSE NIGHT IN HOLLYWOOD

The Hollywood Academy of Medicine devoted its meeting in the Hollywood Roosevelt Hotel, November 14, to a consideration of national defense. Dr. Roy Ledford, San Diego, discussed medical defense; other speakers were Capt. Frederic L. Conklin, M. C., U. S. Navy, chief, surgical service, U. S. Naval Hospital, San Diego; Lieut. Col. Harold V. Raycroft, M. C., U. S. Army, past surgeon, Fort McArthur; Lieut. Col. Dennis W. Sullivan, unit instructor, California National Guard, 160th; Lieut. Comdr. Roy J. Leutscher, M. C., U. S. Navy, chief, medical service, U. S. Naval Hospital, San Diego, and Major John F. Bohlender, M. C., U. S. Army, unit instructor for the medical corps reserve.

BULLETIN OF WAR MEDICINE

As a part of its contribution to medical preparedness, the Medical Research Council of Great Britain has made available a publication called the *Bulletin of War Medicine*, which is a collection of abstracts dealing with the handling of many military-medical affairs, taken from the available medical literature. The first number consists of 62 pages containing 109 abstracts. This Bulletin is available to American readers by addressing the British Library of Information, 50 Rockefeller Plaza, New York. The price is 75 cents per copy.

PUBLIC HEALTH OFFICERS ASSIGNED TO CAMPS

Nine officers of the U. S. Public Health Service have been assigned to the nine U. S. Army corps areas to act as liaison officers with the corps area surgeons especially in problems arising in extra-military areas. Environmental sanitation with emphasis on control of communicable diseases will be their chief responsibility, according to an announcement. The officers assigned are: Drs. Louis L. Williams, Walter T. Harrison, Frank V. Meriwether, Lon O. Weldon, Knox E. Miller, Albert E. Russell, Harry J. Warner, Joseph Bolten and Edgar W. Norris.

MEDICOMILITARY LECTURES IN PHILADELPHIA

A course of lectures on "Military Maxillofacial Surgery" began, November 18, at the Philadelphia County Medical Society Building under the auspices of the Philadelphia County medical and dental societies, the schools of dentistry of the University of Pennsylvania and Temple University and the W. W. Keen Chapter of the Association of Military Surgeons of the United States. The lectures were planned at the request of the surgeon general of the U. S. Army. The first in the series was given by Dr. Oscar V. Batson, professor of anatomy, University of Pennsylvania School of Medicine, and Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania, on "Anatomy of the Face, Jaws and Neck in Relation to War Injuries."

The final lectures in the series presented during the fall by the Philadelphia County Medical Society were as follows:

Lieut.-Col. Asa M. Lehman, Medical Corps, U. S. Army, Noncombatant Military Hospitals and Medical Installations—Civilian Institution Sponsored Hospitals of the Army, November 14.

Dr. Frank W. Burge, The Tuberculosis Problem in the Mobilization of Military and Naval Personnel, November 21.

Lieut. Commander Nathaniel M. Levin, Medical Corps Reserve, U. S. Navy, War Injuries—Air and Food Passages, December 5.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

Following is a list of medical reserve corps officers who had been placed on extended active duty with the regular army by War Department order, Washington, D. C., up until November 8:

ABBAMONTE, Louis Walter, 1st Lieut., Norwich, N. Y.
 ABRAMS, Morris, 1st Lieut., Chicago.
 ADAMS, Eldridge Stevens, Lieut. Col., Washington, D. C.
 ADAMS, George Furman, 1st Lieut., San Francisco.
 AKIN, Robert Louis, 1st Lieut., Monterey, Tenn.
 ALBERTI, Vincent Samuel, 1st Lieut., New York.
 ALBUS, William R., Captain, Fort Sheridan, Ill.
 ALLEN, Robert Wilson, Captain, Keystone, S. D.
 ALLEN, Roy Johnson, 1st Lieut., Sumner, Iowa.
 ALLEN, Samuel, 1st Lieut., East Liverpool, Ohio.
 ALPER, Irwin Isidor, Captain, Ithaca, N. Y.
 AMES, Edward S., 1st Lieut., Forest Hills, N. Y.
 AMLIE, Paul Jones, 1st Lieut., Tripoli, Iowa.
 AMSTER, Milton William, Captain, Brooklyn.
 ANDERSON, John Leonard, Captain, Osceola, Iowa.
 ANDERSON, Edgar Emmet, Captain, Marysville, Kan.
 ANGELL, Howard Hathaway, 1st Lieut., Detroit.
 ANGELLA, Carl Louis, 1st Lieut., Roseville, Calif.
 APONTE, Pedro Rivera, Captain, Fajardo, P. R.
 ARNISTEAD, William Wilchia, Captain, Shreveport, La.
 ARNOLDI, Louis Bernhard, 1st Lieut., New Orleans.
 ARONOFF, Solomon, 1st Lieut., Hoboken, N. J.
 ASCHIER, David Samuel, 1st Lieut., Boston.
 ASHTON, Paul Louis, 1st Lieut., San Francisco.
 AUERBACH, Sidney, 1st Lieut., New York.
 AUSTER, Benjamin, 1st Lieut., Bronx, N. Y.
 AYNER, Saul Leighton, Captain, Savannah, Ga.
 AYERS, Robert Lawrence, 1st Lieut., Pennegrove, Calif.
 AZORIN, Louis Arthur, 1st Lieut., Omaha.
 BACH, Leo Francis, Captain, Mapleton, Minn.
 BADGER, Edward Bruce, Captain, Minneapolis.
 BAER, Erwin Jerome, 1st Lieut., Seattle.
 BAERS, Harry, 1st Lieut., St. Louis.
 BAIRD, Robert Desmond, Jr., 1st Lieut., Edwardsville, Ill.
 BALKO, Andrew John, Captain, El Paso, Texas.
 BALLWEG, Harry Albert, Captain, Brooklyn.
 BAMBACE, Felix Shelley, Captain, Spokane, Wash.
 BARBER, Herbert Gordon, 1st Lieut., Omaha.
 BARKS, Orville Leon, 1st Lieut., Groveland, Fla.
 BARRETT, Robert Syer, 1st Lieut., Hamlin, W. Va.
 BARTOLINI, Frank Joseph, 1st Lieut., Phillipsburg, N. J.
 BAXTER, Clarence Pennell, Lieut. Col., San Diego, Calif.
 BEATY, Charles Samuel, 1st Lieut., Cherokee, Okla.
 BECKER, Harry Gregory, Captain, Evanston, Ill.
 HEGLEY, Philip Jones, 1st Lieut., Hyden, Ky.
 BELL, Allan Brooks, 1st Lieut., Shelton, Wash.
 BELL, Herbert Joseph, Captain, Denver.
 BELL, Robert Stanton, 1st Lieut., Ollie, Iowa.
 BELZ, Joseph A., Captain, Baltimore.
 BENENSON, Abram S., 1st Lieut., East Rockaway, N. Y.
 BENNETT, Bruce Hardy, 1st Lieut., Washington, D. C.
 BENNETT, Webster William, 1st Lieut., Harrisburg, Pa.
 BENNETT, William Horace, 1st Lieut., Paris, Ark.
 BERG, Philip, Jr., 1st Lieut., Philadelphia.
 BERGMAN, Harold Hanford, 1st Lieut., Gillette, Wyo.
 BERLINER, Harry Morris, Captain, Bronx, N. Y.
 BIER, Robert Allen, Captain, Washington, D. C.
 BISKIND, Gerson Ravinson, 1st Lieut., San Francisco.
 BLACK, Benjamin Stephen, 1st Lieut., Rochester, N. Y.
 BLACKSOM, Berget Henri, Jr., 1st Lieut., Rockford, Ill.
 BLOEMENDAAL, Edwin G. J., Captain, Orange City, Iowa.
 BOBES, Solomon Subere, Captain, Wheeling, W. Va.
 BOCHIENEK, John Edward, 1st Lieut., Newark, N. J.
 BODEN, Worthey Carl, 1st Lieut., Davenport, Iowa.
 BOLTON, Ralph Daniel, 1st Lieut., Canton, Ohio.
 BONSIGNORE, Marco Romolo, 1st Lieut., Rochester, N. Y.
 BOROS, Harold Henry, 1st Lieut., Chicago.
 BOSLOW, Harold Meyer, 1st Lieut., Appalachia, Va.
 BOUCHER, Adore Louis, 1st Lieut., Denver.
 BOURIAND, Philip Ewing MacIntyre, 1st Lieut., Calumet, Mich.
 BOYDSTONE, Joseph Oscar, Captain, Hot Springs, Ark.
 BRADLEY, Harold John, 1st Lieut., Brevard, N. C.
 BRADY, Richard Randall, Captain, Tacoma, Wash.
 BRAMBLE, Russell Blaine, Captain, South San Francisco, Calif.
 BRENNER, William Rush, 1st Lieut., Bazine, Kan.
 BRESLIN, John Francis, Captain, Bridgeport, Pa.
 BRIGHT, Albert Seymour, 1st Lieut., Silver Spring, Md.
 BRIMSON, James Ashton, 1st Lieut., Welfare Island, N. Y.
 BRIN, Alfred Ross, 1st Lieut., Terrell, Texas.
 BRISTOL, Frank Ernest, Jr., 1st Lieut., Summit, N. J.
 BRITTON, Bryce Hill, Captain, El Paso, Texas.
 BROCKMAN, Sidney Clark, 1st Lieut., Louisville, Ky.
 BRODERICK, Thomas Aloysius, 1st Lieut., San Francisco.
 BROOKS, Robert Hancy, 1st Lieut., Celeste, Texas.
 BROTHNER, Robert Jacob, 1st Lieut., St. Paul.
 BROTMAN, Jacob H., Captain, Corsicana, Texas.
 BROWN, Charles Thomas, Captain, San Marcos, Texas.
 BROWN, John Edward, Jr., Captain, Blue Mountain, Miss.
 BROWN, Otto Richard, Captain, Los Angeles.
 BROWN, Raymond Milton, 1st Lieut., San Francisco.
 BROWN, Robert Andrew, Jr., 1st Lieut., Greenville, S. C.
 BRUNO, Nicholas Joseph, 1st Lieut., Stambaugh, Mich.
 BRUSSELL, Albert Sinai, Captain, St. Paul.
 BRUTON, Ogden Carr, Captain, Nashville, Tenn.
 BRYANT, Mason David, Jr., 1st Lieut., Lowell, Mass.
 BUCKHOLD, Wilbert William, 1st Lieut., Brandenburg, Ky.
 BUCKHOLTS, Walter Howell, Captain, Elephant Butte, N. M.
 BUERMANN, Henry, Jr., 1st Lieut., Maplewood, N. J.
 BURKS, Arthur Lynn, 1st Lieut., San Francisco.
 BURNETT, Jack Frost, 1st Lieut., Ennis, Texas.
 BURPEAU, William Purdy, Captain, East Orange, N. J.
 BURSTEIN, Henry Albert, Captain, Toledo, Ohio.
 BURTON, Horace French, 1st Lieut., East Tawas, Mich.
 BUSH, Glendon Joseph, 1st Lieut., Detroit.
 BUTMAN, Burton Brooker, 1st Lieut., Syracuse, N. Y.
 BLARS, Perry J. C., 1st Lieut., Lampasas, Texas.
 BYARS, Jerry J. C., 1st Lieut., Lampasas, Tex.
 CACCIATORE, Thomas Joseph, 1st Lieut., Brooklyn.
 CADA, Edward George, 1st Lieut., Berwyn, Ill.
 CALARCO, John Joseph, 1st Lieut., Jamaica, N. Y.
 CAMARDELLA, Ralph Andrew, 1st Lieut., Lynbrook, N. Y.
 CAMPBELL, Joseph Lester, Captain, Ulster, Pa.
 CANNON, Edward Gaine, Captain, Hope Mills, N. C.
 CALLAWAY, James Willis, Captain, La Jolla, Calif.
 CANTRELL, Roy Hammond, Captain, Dallas, Texas.
 CAPALBO, Sylvester Alfred, 1st Lieut., Philadelphia.
 CAPOLA, Michael Thomas, Jr., 1st Lieut., Philadelphia.
 CARDONA, Angel Antonio, Captain, Washington, D. C.
 CAROFIGLIO, Louis Edward, Captain, Chicago.
 CARROLL, Charles Thomas, 1st Lieut., Yonkers, N. Y.
 CASSEL, Melvin Alfred, 1st Lieut., St. Louis.
 CASSIDY, John M., Captain, Chandler, Okla.
 CAVENDER, Savino Walter, 1st Lieut., St. Louis.
 CHAMPION, Walton Thomas, 1st Lieut., Gillett, Ark.
 CLAGETT, Augustus Henry, Jr., Captain, Providence, R. I.
 CLAIBORNE, John Wallons, Jr., Captain, Fort Oglethorpe, Ga.
 CLARKE, Charles Luther, 1st Lieut., Memphis, Tenn.
 CLARKE, Lloyd Anton, 1st Lieut., Kenmore, N. Y.
 CLIFF, Arthur Edgar, Captain, Washington, D. C.
 CHAPPELL, Ewin Summers, 1st Lieut., Washington, D. C.
 COGAN, Leo Judas, Captain, Milwaukee.
 COHEN, Lawrence Jack, 1st Lieut., Baltimore.
 COHEN, Leon John, 1st Lieut., Bronx, N. Y.
 COLEMAN, William Richard, 1st Lieut., Torrington, Wyo.
 COLPOYS, William Patrick, Jr., 1st Lieut., Dorchester, Mass.
 COLQUITT, Alfred Olin, Jr., 1st Lieut., Spartansburg, S. C.
 COLUCCI, David Dominic, 1st Lieut., Rochester, N. Y.
 COLVIN, Paul Verlander, 1st Lieut., Longview, Texas.
 CONNER, Cooper Marion, 1st Lieut., Fort Worth, Texas.
 COONE, Herbert William, 1st Lieut., Providence, R. I.
 CORGILL, Donald Alton, 1st Lieut., Monticello, N. Y.
 COSTRINO, Joseph Alfred, 1st Lieut., St. Louis.
 CRAFTS, John Gardner Hale, Captain, San Francisco.
 CRAWFORD, James Marion, 1st Lieut., New Albany, Miss.
 CRUTCHER, Luke Fain, 1st Lieut., Los Angeles.
 CUMMING, Richard Cralle, Captain, Ocala, Fla.
 CURRIE, Daniel Smith, Jr., 1st Lieut., Parkton, N. C.
 CURTIS, Morris Williams, Captain, Williamsport, Pa.
 CUVILLIER, Louis Marshall, Jr., 1st Lieut., Washington, D. C.
 DAILEY, Jeremiah Aloysius, Captain, El Paso, Texas.
 D'ALFONSO, Anthony Daniel, 1st Lieut., Philadelphia.
 DAMERON, James Haden, Major, Livingston, Texas.
 DAMIAN, Julius Daniel, 1st Lieut., Washington, D. C.
 DANIELS, Elijah Robert, 1st Lieut., Orange, Calif.
 DANIELS, John Quincy Adams, Captain, Portland, Ore.
 DANISHEK, Emil Stephan, 1st Lieut., Seattle.
 DART, Merrill Oren, 1st Lieut., Denver.
 DATZ, Lewis Anthony, 1st Lieut., Pueblo, Colo.
 DAVENPORT, John Robert, Captain, Holdenville, Okla.
 DAVIDSON, Harold Jack, 1st Lieut., Tulsa, Okla.
 DAVIDSON, Morris, 1st Lieut., Elkhart, Ind.
 DAVIES, Dale Henley, 1st Lieut., Seattle.
 DAVIS, Elmer Louis, Captain, Floresville, Texas.
 DAVISON, Augustus Marion, 1st Lieut., Fayetteville, Ark.
 DEL GIUDICE, Amore, 1st Lieut., Waterbury, Vt.
 DELLINGER, Raiden Winfield, 1st Lieut., Rome, Ga.
 DETER, Dwight Meyer, Captain, Austin, Texas.
 DEUTSCH, Albert Leopold, 1st Lieut., Brooklyn.
 DeVAN, William Todd, II, 1st Lieut., Philadelphia.
 DeVITA, Jacob, 1st Lieut., Brooklyn.
 DeVITTORIO, Armond Anthony, 1st Lieut., Ridgeway, Pa.
 DIAMOND, Bernard Lee, 1st Lieut., Ann Arbor, Mich.
 DIAMOND, Max Myer, 1st Lieut., Galveston, Texas.
 DICKINSON, Louis Everett, Jr., 1st Lieut., Ravenna, Neb.
 DIEHL, Earl Henry, Captain, Dunedin, Fla.
 DIGANGI, Mariano Richard, 1st Lieut., Brooklyn.
 DILWORTH, Warren Miller, 1st Lieut., Omaha.
 DINES, George Louis, 1st Lieut., Caropolis, Pa.
 DISARIO, Anthony Ryham, 1st Lieut., Philadelphia.
 DODSON, Charles Albert, Captain, Los Angeles.
 DOHERTY, William Robert, 1st Lieut., Tuscaloosa, Ala.
 DRESCHER, Emmett Burk, Captain, St. Louis.
 DRUMMOND, N. Robert, 1st Lieut., Oklahoma City.
 DUNCAN, Robert Whitworth, 1st Lieut., Fort Worth, Texas.
 DURANT, John Ernest Cameron, 1st Lieut., New Bedford, Mass.
 DUSHANE, Joseph Edward, 1st Lieut., Haverhill, Mass.
 EAKER, Alan Bayliss, 1st Lieut., San Francisco.
 EASTMAN, Wilfred W. Jr., Washington, D. C.
 EASTMAN, Sylvester King, 1st Lieut., Emery, Utah.
 EBY, Robert Elwood, 1st Lieut., New Rochelle, N. Y.
 ECKSTEIN, Albert, 1st Lieut., Staten Island, N. Y.
 EDWARDS, Walton Merideth, 1st Lieut., Oakland, Calif.

MEDICAL PREPAREDNESS

11

EINHORN, Harold, 1st Lieut., Chicago.
 ELKINS, Marvin G., Jr., 1st Lieut., El Reno, Okla.
 EMERSON, Oliver Wayne, 1st Lieut., Junction City, La.
 EMERSON, George Oliver, Jr., Tavares, Fla.
 EPERJESSY, Ernest Zoltan, 1st Lieut., Ontario, Calif.
 EPSTEIN, Carl Charles, 1st Lieut., St. Louis.
 EPSTEIN, Ernest Walfred, 1st Lieut., Sioux City, Iowa.
 ERICKSON, John David, 1st Lieut., Binghamton, Ark.
 ERSHLER, Irving, 1st Lieut., St. Y.
 ERVIN, Clinton Vaughan, Jr., 1st Lieut., San Francisco.
 FABER, Max, Captain, Chelsea, Mass.
 FALKER, John Michael, 1st Lieut., Mount Carmel, Pa.
 FAZIO, Michael George, 1st Lieut., Deaver, Wyo.
 FELDMAN, Max, 1st Lieut., Brooklyn.
 FIMAN, Charles Elden, 1st Lieut., Brooklyn.
 FINKELSTEIN, Benjamin Herman, Captain, Brooklyn.
 FINKELSTEIN, Paul, 1st Lieut., Center, Texas.
 FISHMAN, Louis, Captain, Pottsville, Pa.
 FITZGERALD, Brice E., 1st Lieut., Indianapolis.
 FLAIG, Julian Vincent, Captain, Beverly Hills, Calif.
 FLEMING, Forest Elroy, Captain, Philadelphia.
 FLYGELMAN, Maurice Teller, 1st Lieut., Phoenix City, Ala.
 FLOYD, Cyril Franklin, Captain, El Paso, Texas.
 FOGARTY, Charles James, Captain, Omaha.
 FORTERZA, Resendo, Jr., 1st Lieut., Columbus, Ohio.
 FOSTER, Furman Lamar, 1st Lieut., Hico, La.
 FOX, Lester Irving, 1st Lieut., Quincy, Mass.
 FRANCIS, Vincent D., 1st Lieut., Philadelphia.
 FRANKEL, Leon Allyn, 1st Lieut., Marysville, Calif.
 FRATIS, Anthony Morris, Jr., 1st Lieut., Columbus, Ohio.
 FREED, Albert Edward, 1st Lieut., Tacoma Park, Md.
 FREEDMAN, Mark Abraham, 1st Lieut., Minneapolis.
 FRENCH, James Benjamin, 1st Lieut., Norwich, Conn.
 FRIEDMAN, Harry Samuel, 1st Lieut., Chicago.
 FULGHUM, Thomas Edward, 1st Lieut., Philadelphia.
 GAHM, Irvin George, 1st Lieut., Philadelphia.
 GAMET, Joseph Hiram, Captain, Philadelphia.
 GANSMAN, David Henry, 1st Lieut., Philadelphia.
 GARCIA, Charles Todd, 1st Lieut., Philadelphia.
 GARDNER, Wray Rodgers, Captain, Philadelphia.
 GARTHE, John Joseph, 1st Lieut., Philadelphia.
 GASS, Charles Craig, 1st Lieut., Philadelphia.
 GATTO, Lucio Ernest, 1st Lieut., Philadelphia.
 GENTRY, Thomas Christy, 1st Lieut., Philadelphia.
 GERINGER, Benjamin, 1st Lieut., Philadelphia.
 GESSER, Udell Mathews, 1st Lieut., Philadelphia.
 GIEGERICH, Walter Frank, 1st Lieut., Philadelphia.
 GHOLSEN, Sidney Norman, 1st Lieut., Philadelphia.
 GIBSON, Frank Eugene, 1st Lieut., Philadelphia.
 GILL, Ronald Monroe, 1st Lieut., Philadelphia.
 GILLIAM, Robert Lindsay, Captain, Philadelphia.
 GILMORE, John Edwin, 1st Lieut., Philadelphia.
 GLADSDEN, Eugene Solomon, 1st Lieut., Philadelphia.
 GLAUBMAN, William Aaron, 1st Lieut., Philadelphia.
 GLESON, George LaNore, 1st Lieut., Philadelphia.
 GLICK, Herbert Dudley, Captain, Philadelphia.
 GLICKSMAN, Herbert Yuni, 1st Lieut., Philadelphia.
 GLUCKMAN, Earl Charles, 1st Lieut., Philadelphia.
 GOLD, David, 1st Lieut., Philadelphia.
 GOLDBERG, Louis, 1st Lieut., Philadelphia.
 GOLDEN, Alfred, 1st Lieut., Philadelphia.
 GOLDMAN, David A., 1st Lieut., Philadelphia.
 GOLDMAN, Irving Ralph, 1st Lieut., Philadelphia.
 GOLDSMITH, Irwin Robert, Captain, Philadelphia.
 GOOD, Wealthy William, Captain, Philadelphia.
 GORDON, Everett Julius, 1st Lieut., Philadelphia.
 GRAY, James Harrison, Captain, Philadelphia.
 GRAYSON, Morris, 1st Lieut., Philadelphia.
 GREEN, Arthur Horace, Jr., 1st Lieut., Philadelphia.
 GREEN, George Joseph, Captain, Philadelphia.
 GREENWOOD, Libburn Silva, Captain, Philadelphia.
 GRIGGS, Oscar Broughton, Captain, Philadelphia.
 GROLLMAN, Jaye Jacob, 1st Lieut., Philadelphia.
 GUMPORT, Stephen Lawrence, 1st Lieut., Philadelphia.
 HAAS, William Reid, 1st Lieut., Philadelphia.
 HAIGLEY, Thomas Brien, Captain, Philadelphia.
 HALE, Clayton H., 1st Lieut., Philadelphia.
 HALLINGER, Earl Stephen, Jr., 1st Lieut., Philadelphia.
 HALPERIN, Louis, 1st Lieut., Philadelphia.
 HALPERIN, Meyer, 1st Lieut., Philadelphia.
 HAM, George Hilary, Captain, Philadelphia.
 HAMEL, Paul Raymond, 1st Lieut., Philadelphia.
 HAMM, Leshe Thompson, 1st Lieut., Philadelphia.
 HAMMATT, Harold Wayne, 1st Lieut., Philadelphia.
 HANSELL, Robert Joseph, Captain, Philadelphia.
 HANSEN, Paul George, Captain, Philadelphia.
 HANSON, Lawrence Benton, Captain, Philadelphia.
 HARPER, Kenneth Joseph, Captain, Philadelphia.
 HARRIS, Edwin Oliver, Captain, Philadelphia.
 HARTLAND, William C., Captain, Philadelphia.
 HARTMAN, Jack, 1st Lieut., Philadelphia.
 HARTMAN, Owen Wister, 1st Lieut., Philadelphia.
 HARVEY, Bernard Joy, 1st Lieut., Philadelphia.
 HARWITZ, Morris, 1st Lieut., Philadelphia.
 HAYDEN, Sherman Reward, Captain, Philadelphia.
 HEDERICK, Rogers, 1st Lieut., Philadelphia.
 HEDGE, Arden Russell, 1st Lieut., Philadelphia.
 HEFFERNON, George Allen, Captain, Philadelphia.

HEGER, Frank Ferdinand, Captain, Shiner, Texas.
 HEINITSH, George, 1st Lieut., Fayetteville, N. C.
 HELLER, Harold, 1st Lieut., San Jose, Calif.
 HELLER, Morris Isadore, 1st Lieut., Cleveland.
 HENRY, Joseph Raymond, 1st Lieut., Detroit.
 HENTON, George Herbert, Captain, Portland, Ore.
 HERMAN, Julius, 1st Lieut., Fort Wayne, Ind.
 HERMES, Richard Lawrence, 1st Lieut., Fort Worth, Texas.
 HERNDON, Gilbert Cole, 1st Lieut., Chelsea, Mass.
 HICKS, George Yeger, Captain, St. Louis.
 HO, Kwan Heen, Captain, St. Louis.
 HOFFMAN, Archie Arthur, 1st Lieut., Chelsea, Mass.
 HOFFMAN, Charles Wilbur, Jr., 1st Lieut., Baltimore.
 HOLDEN, Howard Thompson, 1st Lieut., Rabun Gap, Ga.
 HOLLAND, Robert Mannix, 1st Lieut., West Roxbury, Mass.
 HOLLINGSWORTH, Charles Edward, 1st Lieut., Chickasha, Okla.
 HOLMES, Michael, Captain, Fort Moultrie, S. C.
 HOPPENSTEIN, Eugene Samuel, 1st Lieut., Philadelphia.
 HORSMAN, Russell Keaten, 1st Lieut., Los Angeles.
 HRENOFF, Joseph, 1st Lieut., San Francisco.
 HUBBARD, Ralph Waldo, 1st Lieut., Oklahoma City.
 HUNT, Walter Skellie, Jr., 1st Lieut., Raleigh, N. C.
 HYMAN, Daniel, 1st Lieut., Washington, D. C.
 ISHAM, Charles Augustus, 1st Lieut., San Francisco.
 JACOBS, Frederick Matthews, 1st Lieut., Roanoke, Va.
 JACOBS, Herbert M., 1st Lieut., Cleveland.
 JEWELL, James Harlan, Captain, Racine, Wis.
 JOHNSON, Carroll Allen, Jr., 1st Lieut., Marfa, Texas.
 JOHNSON, Cyrus Cleveland, 1st Lieut., Greenville, Miss.
 JUSTER, Milton Alter, Captain, South Bend, Ind.
 JUSTICE, Frank K., Captain, Washington, D. C.
 KABAHER, Charles Bernard, 1st Lieut., Lexington, Ky.
 KAFKA, Adolf Joseph, 1st Lieut., Scotia, Neb.
 KAMESIS, John Joseph, 1st Lieut., Cleveland.
 KANNER, Morris, 1st Lieut., Philadelphia.
 KAPLAN, Albert Jordan, 1st Lieut., Philadelphia.
 KAPLAN, Ronald R., 1st Lieut., Cleveland Heights, Ohio.
 KAREL, Jack R., Captain, Tacoma, Wash.
 KASSAN, Robert Jacob, 1st Lieut., Washington, D. C.
 KAUFMAN, Abraham Saul, 1st Lieut., Philadelphia.
 KAYNE, Jerry, 1st Lieut., Chicago.
 KELLY, Miles William, 1st Lieut., New York.
 KELLY, Sylvester Mechan, 1st Lieut., Fort Benning, Ga.
 KEMP, Milton, 1st Lieut., Fort Benning, Ga.
 KENT, Clifford Foster, Captain, Kansas City, Kan.
 KETCHUM, Eugene Linwood, 1st Lieut., Forsyth, Ga.
 KING, James Thomas, 1st Lieut., Valosta, Ga.
 KISNER, Paul, Captain, Fort Snelling, Minn.
 KNAUF, George Milton, 1st Lieut., Rising Sun, Md.
 KNECHT, Edward M., 1st Lieut., Philadelphia.
 KNESE, Luke Ambrose, Captain, Billings, Mont.
 KOEBERT, Martin Joseph, 1st Lieut., Philadelphia.
 KOSTECKI, Walter Andrew, 1st Lieut., Schenectady, N. Y.
 KRIEGER, Howard Gottlieb, 1st Lieut., Schenectady, N. Y.
 KROSNICK, Gerald, 1st Lieut., New Haven, Conn.
 KUHN, John J., 1st Lieut., Cambridge, Mass.
 KRAJESKI, Delphin Stanley, 1st Lieut., Wilkes-Barre, Pa.
 KRAUBER, Samuel, 1st Lieut., Fayetteville, N. C.
 LACKAY, Raleigh Howard, 1st Lieut., Kansas City, Mo.
 LAMAR, Robert Frederick, 1st Lieut., Vancouver, Wash.
 LAMY, John Ernst, 1st Lieut., Chicago.
 LARAWAY, Thurston William, Captain, Philadelphia.
 LASNER, Jack, 1st Lieut., Philadelphia.
 LAUER, David Patrick, 1st Lieut., Philadelphia.
 LAWLOR, John Martin, 1st Lieut., Philadelphia.
 LEE, Albert Ray, 1st Lieut., Philadelphia.
 LEE, Jack Bennett, 1st Lieut., Dallas, Texas.
 LEVINS, Leo Victor, 1st Lieut., Hot Springs National Park, Ark.
 LEVISOHN, Milton Jack, 1st Lieut., Chicago.
 LIDE, Thomas Norwood, 1st Lieut., Washington, D. C.
 LEIBOWITZ, Hyman, 1st Lieut., Brooklyn.
 LEICHTER, Martin, 1st Lieut., Shively, Ky.
 LERNER, Philip, 1st Lieut., Chicago.
 LERNER, Vincent, Captain, South Minneapolis, Minn.
 LIPMAN, Bernard John, Jr., Captain, Philadelphia.
 LIPMAN, Nathan Lewis, 1st Lieut., Atlantic City, N. J.
 LITTLETON, William Henry, 1st Lieut., Estes Park, Colo.
 LOCHEN, Everett Lee, Captain, Waukesha, Wis.
 LONG, Gerald A., 1st Lieut., Detroit.
 LORANGER, Guy Lincoln, 1st Lieut., Omaha.
 LOUDON, James Frederick, 1st Lieut., Columbus, Ohio.
 LOVEBURY, William Frederick, 1st Lieut., Big Horn, Wyo.
 LOVE, Stanton Clifford, 1st Lieut., Potomac, Okla.
 LOWREY, Robert Wayne, 1st Lieut., St. Louis.
 LUEDDE, John Robert Woods, 1st Lieut., Leupp, Ariz.
 LUKAS, Edward Albert, 1st Lieut., Redding, Calif.
 LUPARELLO, Thomas Gaetano, Captain, Denver.
 LURIA, Sydney, 1st Lieut., Brevard, N. C.
 LYDAY, Wilson, 1st Lieut., Fort Worth, Texas.
 LYMAN, Irving Richard, 1st Lieut., Sequin, Texas.
 LYONS, Robert Edward, 1st Lieut., San Antonio, Texas.
 McANALLY, William Jefferson, Jr., 1st Lieut., High Point, N. C.
 McCARROLL, William Harold, 1st Lieut., Yerington, Nev.

McCLINTOCK, John Laughlin, 1st Lieut., Philadelphia.
 McCoy, States Donald, Captain, Columbus, Ohio.
 McCREADY, Robert Bruce, 1st Lieut., Chicago.
 McDERMOTT, Robert West, 1st Lieut., Munhall, Pa.
 McDONOUGH, Joseph Francis, 1st Lieut., Palo Alto, Calif.
 McDOWELL, James Frederick, Captain, Birmingham, Ala.
 McGRAW, John Phillip, 1st Lieut., Estes Park, Colo.
 McGUINNESS, Joseph Stanley, 1st Lieut., San Francisco.
 McHALE, Donald Gareth, 1st Lieut., Miami, Fla.
 McKEE, Robert Doreck, 1st Lieut., San Antonio, Texas.
 McKISSICK, John Campbell, Captain, Paris, Tenn.
 McMANUS, James William, Jr., Captain, Laurel, Md.
 McQUEEN, Max Boyd, Captain, Lewiston, Ida.
 McREE, Walter Everett, 1st Lieut., Port Arthur, Texas.
 MACK, Joseph John, Captain, Little Rock, Ark.
 MADOFF, Irving, Captain, New York.
 MAGUDA, Thomas Andrew, 1st Lieut., Sheatown, Pa.
 MAKOVSKY, Irwin Harry, Captain, St. Louis.
 MANGIMELLI, Samuel Thomas, 1st Lieut., Omaha.
 MANNING, John Gilbert, 1st Lieut., Los Angeles.
 MARESH, Gerald Stanley, 1st Lieut., Iowa City.
 MARINACCI, Albert Antonio, 1st Lieut., Los Angeles.
 MARKER, Daniel Isaac, Captain, Manhattan, Kan.
 MARKS, Maurice Isaac, Jr., 1st Lieut., Atlanta, Ga.
 MARROCCO, William Alexander, Captain, Paterson, N. J.
 MARSICO, John, 1st Lieut., Lorain, Ohio.
 MARTIN, Farris James, 1st Lieut., Montgomery, Ala.
 MARTIN, Richard Dorr, 1st Lieut., Detroit.
 MASLER, Sherman, 1st Lieut., Van Nuys, Calif.
 MASCARO, Joseph Raymond, Captain, Utica, N. Y.
 MASON, David, 1st Lieut., Lewiston, Ida.
 MATTHIS, Austin Wood, Captain, Darrouzett, Texas.
 MAUPIN, Clinton Shockey, 1st Lieut., Waurika, Okla.
 MELANCON, Joseph Francis, 1st Lieut., St. Paul.
 MENCHER, Edward Wallace, 1st Lieut., New York.
 MERMIS, William Leo, Captain, Centaur Station, Mo.
 MESSINA, Domenic Sebastian, 1st Lieut., Buffalo.
 MEYER, Morton Arthur, 1st Lieut., San Francisco.
 MICKEL, Arthur Adams, 1st Lieut., Lomita, Calif.
 MILFORD, Albert Findley, 1st Lieut., Ann Arbor, Mich.
 MILLER, Jack Eaton, 1st Lieut., Oklahoma City.
 MILLER, Lee Edward, 1st Lieut., Milwaukee.
 MILTON, Paul Harold, Captain, Decatur, Ga.
 MIRSKY, Louis Halliday, 1st Lieut., Brooklyn.
 MONTGOMERY, John Willard, 1st Lieut., Pasadena, Calif.
 MITCHELL, Robert Hiestand, 1st Lieut., Chicago.
 MOONEY, Alfonso John, Jr., 1st Lieut., Statesboro, Ga.
 MOORE, Chester Garfield, Jr., 1st Lieut., San Francisco.
 MORROW, Charles Sol, 1st Lieut., Newark, N. J.
 MOORE, William Andrew, Captain, Olney, Ill.
 MOORE, William Sivley, 1st Lieut., Memphis, Tenn.
 MORGAN, Jack Albert, Captain, Elgin, Ill.
 MORRISON, Marcus Eugene, 1st Lieut., Oxford, Miss.
 MOUNCE, Chanceford Afton, 1st Lieut., Lynwood, Calif.
 MOYER, Leonard Byron, Captain, Carson, N. D.
 MOZERSKY, Victor, 1st Lieut., San Antonio, Texas.
 MUCKLE, Craig Wright, Captain, Haverford, Pa.
 MULFORD, Todd Merriam, 1st Lieut., Los Angeles.
 MUNDT, Raymond, Captain, Juneau, Alaska.
 MURPHY, John Thomas, 1st Lieut., Green Bay, Wis.
 NABBE, Philip Morris, 1st Lieut., Chicago.
 NAGLER, J. Herbert, 1st Lieut., Philadelphia.
 NEBINGER, Rankin Arthur, Captain, Lexington, Miss.
 NELSON, Robert Burwell, Jr., 1st Lieut., Winchester, Va.
 NEIDICH, Sol, 1st Lieut., Beauford, S. C.
 NETHERY, Sidney J., Jr., 1st Lieut., Belle Mina, Ala.
 NEURWIRTH, Abraham A., Captain, Floral Park, Long Island, N. Y.
 NEWTON, William Howard, Captain, Chicago.
 NICOLETTE, Anthony Joseph, 1st Lieut., Mount Pleasant, Pa.
 NICOSIA, Ralph Vincent, 1st Lieut., Houston, Texas.
 NIXON, Pat Ireland, Jr., 1st Lieut., Washington, D. C.
 NOELL, Livingston Pope, Jr., 1st Lieut., New Orleans.
 NORMAN, Earle Theodore, Captain, Uvalde, Texas.
 NORTHOP, Richard Francis, 1st Lieut., Philadelphia.
 NOVAK, Theodore William, Captain, Columbus, Ohio.
 OAKES, Harold Forest, 1st Lieut., El Paso, Texas.
 O'BRIEN, Frederick E., 1st Lieut., Cambridge, Mass.
 ONDASH, Stephen William, 1st Lieut., Youngstown, Ohio.
 O'NEILL, Francis Edward, 1st Lieut., Sanderson, Texas.
 OPSAHL, Harold Eugene, Captain, Washington, D. C.
 ORTMAN, Gareth Spencer, 1st Lieut., Otego, Kan.
 PAPKIN, George, 1st Lieut., Los Angeles.
 PARKE, Delmar Davis, Captain, Indianapolis.
 PARKER, David Marcellus, Captain, Oakland, Calif.
 PARKS, Harold Darby, Major, Lancaster, Texas.
 PATTERSON, Fred Lindley, Jr., 1st Lieut., Mountain View, Okla.
 PATTON, Thomas Ewing, 1st Lieut., North Jackson, Ohio.
 PAYNE, Royal Chester, Captain, Hollywood, Calif.
 PEARSON, Paul Ernest, 1st Lieut., Kansas City, Mo.
 PEDERSEN, Paul Milton, 1st Lieut., Oakland, Calif.
 PERRI, Frank Adrian, 1st Lieut., Philadelphia.
 PETERSEN, Fenton Joseph, 1st Lieut., Richmond Heights, Mo.
 PETERSON, Wendell Case, 1st Lieut., Fairbury, Neb.
 PIERCE, Richard Kenneth, Captain, San Francisco.
 PIGFORD, Charles Alfred, Captain, Tulsa, Okla.
 PITTMAN, Cole Dilling, Captain, Tulsa, Okla.
 PITTMAN, Wayne Creekmore, Captain, Bay St. Louis, Miss.
 PLESSINGER, Virgil Allen, 1st Lieut., Washington, D. C.
 PLETCHER, Kenneth Eugene, 1st Lieut., Eldon, Mo.
 POHLMAN, David A., Captain, Pasadena, Calif.
 POLLACK, David, 1st Lieut., Columbus, Ohio.
 POPELAR, Melville Valerian, Captain, Omaha.
 POSNER, Sidney, 1st Lieut., Robstown, Texas.
 POTTER, George Vernon, 1st Lieut., Oakland, Calif.
 POWERS, Francis Irving, 1st Lieut., Glendora, Calif.
 PRATT, George Olin, Captain, Richford, Vt.
 PRATT, Harold Ernst, 1st Lieut., San Pedro, Calif.
 PRATT, William Coleman, 1st Lieut., Danville, Pa.
 PROCTOR, Clark Bartlett, Captain, Ames, Iowa.
 PUSHKIN, E. Aaron, 1st Lieut., West Hempstead, N. Y.
 PREWITT, John Hanna, 1st Lieut., Lexington, Ky.
 PRIOR, Frank H., Captain, Colorado Springs, Colo.
 PUZZISS, Abe, 1st Lieut., Portland, Ore.
 QUINE, Robert Corkill, Captain, San Diego, Calif.
 RABINOWITZ, Carl Hirsch, 1st Lieut., New Orleans.
 RABOURN, William Ossian, Captain, Port Byron, N. Y.
 RADLOFF, Frederick F., 1st Lieut., Spokane, Wash.
 RADIVOJEVIC, Sava Mathew, 1st Lieut., Portland, Ore.
 RAFFEL, William, 1st Lieut., Washington, D. C.
 RADZYMINSKI, Stanislas Francis, 1st Lieut., Chicago.
 RATE, Robert Goodwin, 1st Lieut., Santa Barbara, Calif.
 RAY, Louis, 1st Lieut., Tule Lake, Calif.
 RAYMOND, Frank Kondziorski, 1st Lieut., Chicago.
 READINGER, Ivan Henry, 1st Lieut., El Paso, Texas.
 RECUPERO, Joseph Rocco, 1st Lieut., Brooklyn.
 REIGER, John Leslie, 1st Lieut., Craig, Colo.
 REISSMAN, Samuel Gearson, 1st Lieut., Detroit.
 REISSMAN, Seymour, 1st Lieut., Brooklyn.
 REYNOLDS, Francis Henry, 1st Lieut., Columbus, N. M.
 RHYNE, Walter Percival, Captain, Albany, Ga.
 RICHARDS, Lewis Jones, 1st Lieut., Mobile, Ala.
 RICHMOND, Van Rensselaer, 1st Lieut., Welfare Island, N. Y.
 RICKER, Walter Albra, Jr., 1st Lieut., Wauwatosa, Wis.
 RITTER, Morton David, 1st Lieut., Atlantic City, N. J.
 RIVA, Humbert Lewis, 1st Lieut., Charleoi, Pa.
 ROADMAN, Charles Harvey, 1st Lieut., Dallas, Texas.
 ROBBINS, Ben, 1st Lieut., Pittsburgh.
 ROBINSON, Murry Myer, Captain, Washington, D. C.
 ROBINSON, Howard, 1st Lieut., Wayne, Mich.
 ROGOFF, Bernard, 1st Lieut., Ozone Park, N. Y.
 ROTH, Sydney Sigmund, 1st Lieut., Chicago.
 ROSANOVA, Albert Ralph, 1st Lieut., Chicago.
 ROSE, Joseph, Captain, Jacksonville, Fla.
 ROSEN, Samuel Clarence, 1st Lieut., Philadelphia.
 ROSENSTEIN, Samuel William, 1st Lieut., Brooklyn.
 ROSS, James Keener, 1st Lieut., Salisbury, Md.
 ROSS, Samuel, Captain, San Francisco.
 ROUSE, James William Harlow, Captain, San Antonio, Texas.
 ROTHSTEIN, Martin Mayer, 1st Lieut., Philadelphia.
 ROWELL, Forrest Ardell, Jr., 1st Lieut., Boston.
 RUBIN, Herschel Jerome, 1st Lieut., Tulsa, Okla.
 RUBIN, Myron Michael, 1st Lieut., Brooklyn.
 RUBIN, Nathan Samuel, Captain, Pensacola, Fla.
 RULNEY, Max, Captain, New York.
 RUSSELL, Blanton Everett, 1st Lieut., Clinton, Ky.
 RUSSO, Joseph John, Captain, Albany, N. Y.
 RUSS, Stirling Everett, 1st Lieut., San Antonio, Texas.
 SACHS, Maurice David, 1st Lieut., San Francisco.
 SAFFRON, Morris Harold, Captain, Passaic, N. J.
 SALIBA, Nicholas Saloom, 1st Lieut., Walsenburg, Colo.
 SANDERS, Preston Randolph, 1st Lieut., Big Springs, Texas.
 SANDERS, Zal Hyman, 1st Lieut., Rock Island, Ill.
 SANDY, William Allee, Captain, Indianapolis.
 SANJURJO RAMIREZ, Louis Arturo, 1st Lieut., Santurce, P. R.
 SANTANIELLO, William Michael, 1st Lieut., Brooklyn.
 SARKISSIAN, Sarkis Der, Captain, Chicago.
 SAUNDERS, Irvine, 1st Lieut., Bedford, Va.
 SCHAM, Manuel Joseph, Captain, Bronx, N. Y.
 SCHAUMLOFFEL, Roland Abraham, 1st Lieut., Los Angeles.
 SCHIFF, Bence Leib, 1st Lieut., Philadelphia.
 SCHILDHAUS, Andrew Irving Ephraim, 1st Lieut., Shelburne, Vt.
 SCHINDLER, Meyer, 1st Lieut., San Francisco.
 SCHIOWITZ, Albert, 1st Lieut., Wilkes-Barre, Pa.
 SCHLESINGER, Henry A., 1st Lieut., Brooklyn.
 SCHNABEL, Garfield Pickering, Captain, Phoenix, Ariz.
 SCHNEIDER, Louis W., Captain, University City, Mo.
 SCHNELLER, Oscar, 1st Lieut., Woodside, Long Island, N. Y.
 SCHNUR, Sidney, 1st Lieut., Houston, Texas.
 SCHULTZ, John Martin, Captain, West New York, N. J.
 SCHULTZ, Samuel Karl, Captain, Lewistown, Pa.
 SCHUMACHER, George Otto, 1st Lieut., Loma Linda, Calif.
 SCHUTZ, Joe Dulaney, 1st Lieut., San Antonio, Texas.
 SCHWALBE, Nathan Alter, 1st Lieut., Brooklyn.
 SCHWARTZ, Edward Norton, 1st Lieut., St. Louis.
 SEGAL, Robert, 1st Lieut., Lompoc, Calif.
 SEIBLY, Robert Chester, 1st Lieut., Los Angeles.
 SELKOVITS, Sidney Cecil, 1st Lieut., Aliquippa, Pa.
 SELSER, Richard Elijah, Captain, New Orleans.
 SERON, Zaven M., Captain, Sebring, Fla.
 SHEPHERD, Eugene Bowie, 1st Lieut., Richmond, Va.
 SIBLEY, D. Jacobi, Jr., 1st Lieut., Fort Stockton, Texas.
 SIEGEL, Sidney James, 1st Lieut., Brooklyn.
 SILVER, Michael William, 1st Lieut., Paterson, N. J.
 SIMMANG, Arthur Vincent, 1st Lieut., San Antonio, Texas.
 SIMON, Charles, 1st Lieut., Brooklyn.
 SIMON, Sylvan William, Major, Chicago.
 SIMONSON, Sigwert Wallace, 1st Lieut., Dallas, Wis.
 SIRKEN, Joseph Grover, 1st Lieut., Philadelphia.
 SINBURY, Carl Ellwood, Captain, Des Moines, Iowa.
 SKOW, George Dominico, 1st Lieut., Racine, Wis.
 SMITH, Emmett Montgomery, Captain, Dallas, Texas.
 SMITH, George Lafayette, 1st Lieut., Decherd, Tenn.
 SMITH, Norvin Richards, 1st Lieut., Big Springs, Neb.
 SMITH, Tom Jerry, 1st Lieut., Covington, Ky.
 SMOLENS, Nathan Morris, Captain, Philadelphia.
 SMYKA, Edward Joseph, 1st Lieut., Detroit.
 SOHM, John Joseph, 1st Lieut., Memphis, Tenn.
 SOHMER, Abram, 1st Lieut., Jamaica, N. Y.
 SOLTZ, Gustav Deane, 1st Lieut., Denver.
 SPANGLER, Edward Louis, 1st Lieut., Ouray, Colo.
 SPENCER, Jacob John, Major, St. Augustine, Fla.
 SPENCER, James Devore, 1st Lieut., Somerset, Pa.

SPIERER, Eugene, 1st Lieut., Chicago.
SPUNT, Edward Theodore, Captain, Bronx, N. Y.
STAATS, Roydice, 1st Lieut., Cairo, W. Va.
STAPP, Celso C., 1st Lieut., Burnet, Texas.
STARK, Ray Gingles, 1st Lieut., Kirksey, Ky.
STARK, Walter Alfred, Captain, Las Vegas, N. M.
STARR, Wilmer Hyatt, 1st Lieut., Hollywood, Calif.
STEARNS, Horace Ivan, 1st Lieut., Los Angeles.
STEELE, Virgil Shellnut, 1st Lieut., San Antonio, Texas.
STEGEMAN, Abraham Mannes, Captain, Tripoli, Iowa.
STEIN, Ben, 1st Lieut., Ennis, Texas.
STEVENS, Weir Cloyd, 1st Lieut., Los Angeles.
STILLINGER, Cecil George, Captain, Columbus, Ohio.
STINE, George Thomas, 1st Lieut., East Point, Ga.
STONE, Fred D., Captain, Chicago.
STONE, Vean Melford, 1st Lieut., Fort Lewis, Wash.
STORCH, Sidney, 1st Lieut., Brooklyn.
STRAND, Clarence Johnson, Captain, Amherst, Neb.
SULLIVAN, Frederick J., 1st Lieut., Fall River, Mass.
SUMNER, Albert, 1st Lieut., Chicago.
SUTLEY, Percy Hall, 1st Lieut., Baltimore.
SUTTON, James Alva, 1st Lieut., Avonmore, Pa.
SWAN, Joseph Jasper, 1st Lieut., Fort Worth, Texas.
SWANSON, Wendell F., Captain, Knoxville, Tenn.
SWEeley, William Jennings, Captain, Jacksonville, Fla.
SWENSON, Orrin Endre, 1st Lieut., Stoughton, Wis.
SYDOW, Henry, 1st Lieut., Omaha.
SNISCAK, John Michael, 1st Lieut., Philadelphia.
SPRITZLER, Ramon Joseph, 1st Lieut., Philadelphia.
TARPLEE, Scott LaRue, Captain, Atlanta, Ga.
TASCARELLA, James William, 1st Lieut., Brooklyn.
TAVARES, Clement Adams, 1st Lieut., Los Angeles.
TAX, Archie Hanwit, Captain, Milwaukee.
TAYLOR, Owen Hobson, Jr., Captain, Ridgely, Tenn.
THOMAS, David P., 1st Lieut., Elmhurst, Pa.
THOMAS, Henry S., 1st Lieut., Santa Cruz, Calif.
THOMPSON, Marvin Loughran, 1st Lieut., Davenport, N. Y.
THONE, Frank Henry, 1st Lieut., Murray, Utah.
THORNER, Melvin Wilfred, Captain, Philadelphia.
TOBIN, William James, 1st Lieut., Charleston, S. C.
TODD, Hobart Hare, Jr., 1st Lieut., Oak Park, Ill.
TODOROVIC, Dragutin D., Captain, Macdoel, Calif.
TOMPKINS, Harold Phillip, 1st Lieut., Santa Barbara, Calif.
TOWNSEND, Frank Marion, 1st Lieut., New York.
TRACY, Herbert Allen, 1st Lieut., Neodesha, Kan.
TROBOUGH, George Eugene, 1st Lieut., Omaha.
TUTTLE, Jay Forrester, 1st Lieut., Bremerton, Wash.
VANDIVIERE, Stuart Pitner, Captain, Dawsonville, Ga.
VAN MATRE, Reber Miller, Captain, Walters, Okla.
VANNETER, James Clyde, Captain, Columbus, Ohio.
VERSTANDIG, Charles Coleman, 1st Lieut., East Boston, Mass.

FIRST CORPS AREA

The following medical reserve corps officers had been ordered to extended active duty with the regular army by First Corps Area Orders since November 8 and up to midnight, November 16. The First Corps Area comprises the states of Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island and Vermont:

VICKERS, James Edmund, 1st Lieut., San Bernardino, Calif.
VIDA, Alexander, 1st Lieut., Detroit.
VOGEL, Louis Alfred, Captain, Glandorf, Ohio.
VOTAW, Frederick Lee, 1st Lieut., Pittsburgh.
WADDELL, Otto Joseph, Jr., 1st Lieut., Dallas, Texas.
WAGGONER, Harry Nelson, 1st Lieut., Dyersburg, Tenn.
WAINER, Amos Shepherd, 1st Lieut., Philadelphia.
WALKER, Weldon Joseph, 1st Lieut., Los Angeles.
WALL, Malcolm Musgrave, 1st Lieut., Washington, D. C.
WARD, Aaron Cleveland, Captain, Calhoun Falls, S. C.
WARNER, Frank Amel, Captain, Baltimore.
WALBRIGHT, George W., 1st Lieut., Escanaba, Mich.
WASHKO, Peter John, 1st Lieut., Edwardsville, Pa.
WATT, James Andrew, 1st Lieut., Columbus, Miss.
WEBER, John Martin, 1st Lieut., New Rochelle, N. Y.
WEHS, Richard John, Captain, Washington, D. C.
WEISS, Samuel Aaron, Captain, Denver.
WENNERSTEIN, Jack Ralph, 1st Lieut., Pottstown, Pa.
WENTWORTH, John Hall, 1st Lieut., New Haven, Conn.
WEST, Jasper Daniel, Captain, Memphis, Tenn.
WEAVER, Emerson M. F., Captain, Lancaster, Pa.
WIELAND, Wesley William, 1st Lieut., Virginia Beach, Va.
WHITE, Raymond Leroy, 1st Lieut., New Plymouth, Ida.
WESTCOTT, Albert Goodwin, 1st Lieut., San Francisco.
WHISTLER, Carl William, 1st Lieut., El Paso, Texas.
WHITCOMB, Luther Myron, 1st Lieut., Carlisle, Pa.
WHITE, Edgar William, Lieut.-Colonel, New York.
WHITE, Fletcher Howard, 1st Lieut., Burlington, Vt.
WHITE, Gilbert William, Captain, East Prospect, Pa.
WHITE, Thomas Beeman, 1st Lieut., Plain Dealing, La.
WHITMAN, Joseph Jay, Captain, Cleveland.
WHITMER, Lysle Henderson, 1st Lieut., Wilton Junction, Iowa.
WILLIAMS, John Wyley, Captain, Oak Grove, Mo.
WILLIAMS, Russel I., 1st Lieut., Lincoln, Neb.
WILLIGER, Irwin Fox, 1st Lieut., South Harriman, Tenn.
WINGFIELD, William Lynn, 1st Lieut., Ashland, Va.
WOLF, Nathan, 1st Lieut., Baltimore.
WOLFE, Herbert S., Captain, New York.
WONG, James Sin Fook, Captain, Philadelphia.
WRIGHT, Burchard Eakin, Jr., Captain, Philadelphia.
WRIGHT, Garland Miller, 1st Lieut., Harrisonburg, Va.
WRIGHT, Jack McClellan, 1st Lieut., Stillwater, Okla.
WRIGHT, Thomas Rogers, 1st Lieut., El Paso, Texas.
WYLIE, John Thomas, Captain, Dallas, Texas.
YACHNIN, Samuel Cyril, Captain, Lyndhurst, N. J.
YOUNG, Charles Oran, 1st Lieut., San Pedro, Calif.
YOUNG, Richard Wallace, 1st Lieut., Baton Rouge, La.
YOVAISH, Walter, Captain, Germfask, Mich.
ZEFF, Charles, 1st Lieut., New York.
ZOX, Maurice Levi, 1st Lieut., Philadelphia.
ZWEIBEL, Leonard, 1st Lieut., Newark, N. J.

FOURTH CORPS AREA

The following medical reserve corps officers have been ordered to active duty by Fourth Corps Area Order since November 8. The Fourth Corps Area comprises the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana.

ABRAM, Lewis E., 1st Lieut., Fitzgerald, Ga.
ARNOLD, Laurie J., Jr., 1st Lieut., Lake City, Fla.
ARP, Charles R., 1st Lieut., Atlanta, Ga.
ARTEAGA, Oliver, 1st Lieut., Atlanta, Ga., Camp Blanding, Fla.
BARFIELD, Hugh H., 1st Lieut., Atlanta, Ga.
BARNWELL, Edward H., Lieut. Col., Charleston County, S. C.
BERRY, John L., Captain, Miami, Fla., Savannah A. A. Firing Center, Savannah, Ga.
BICHARD, Phillip M., 1st Lieut., Orlando, Fla.
BLEICH, Jack K., Captain, Atlanta, Ga.
BUCKLEY, Madison H., 1st Lieut., Martin, Tenn., Camp Peay, Tullahoma, Tenn.
BURGE, Julius C., Jr., 1st Lieut., Black Mountain, N. C., Camp Peay, Tullahoma, Tenn.
CASTELLOW, William F., Captain, Americus, Ga.
CHEW, Nathaniel J., 1st Lieut., Bristol, Tenn.
COLLINS, Braswell E., 1st Lieut., Waycross, Ga., Camp Blanding, Fla.
CONNOR, John M., 1st Lieut., Panama City, Fla., Camp Blanding, Fla.
DUCKWELL, Fred M., 1st Lieut., Kingsport, Tenn.
EDELSON, Edmond K., 1st Lieut., New Orleans.
FARRAR, Turley, 1st Lieut., Memphis, Tenn.
FITZGERALD, Charles E., 1st Lieut., Farmville, N. C., Camp Beauregard, La.
GEESELYN, Lawrence E., 1st Lieut., Atlanta, Ga.
HALLOWAY, Charles E., 1st Lieut., Atlanta, Ga.
HARRELL, Henry L., Captain, Ocala, Fla.

ALLMAN, Sydney J., 1st Lieut., Mattapan, Mass.
FAGONE, Francis A., 1st Lieut., Portland, Maine.
FAMULARO, Nicholas A., Lieut., Jackman, Maine.
GORMAN, Richard J., Lieut., Winchendon, Mass.
HEELS, George E., Lieut., Cambridge, Mass.
NELSON, John A., Lieut., Augusta, Maine.
SHERMAN, Bernard I., Captain, Providence, R. I.
SHUMAN, Harold I., 1st Lieut., Brookline, Mass.
WILLSON, Allan T., Lieut., Farmington, N. H.

HARRISON, Albertus F., 1st Lieut., Florence, S. C., Savannah A. A. Firing Center, Savannah, Ga.
HOLLIDAY, Henry C., 1st Lieut., Athens, Ga.
HOUSTON, John L., 1st Lieut., Memphis, Tenn.
KENNEDY, Leon T., Captain, Winston-Salem, N. C.
KRONRAD, Lorenz, 1st Lieut., Columbia, S. C., Camp Beauregard, La.
LEVY, Tracy, 1st Lieut., New Orleans, Savannah A. A. Firing Center, Savannah, Ga.
MASON, George S., 1st Lieut., Lumberton, Miss.
McCORD, William M., 1st Lieut., New Orleans, Camp Beauregard, La.
McCRAVEY, Augustus, 1st Lieut., Whitestone, Ga.
McNABB, John T., 1st Lieut., Whitwell, Tenn., Savannah A. A. Firing Center, Savannah, Ga.
MUSE, William S., 1st Lieut., Knoxville, Tenn.
OWENS, Bennett G., Major, Valdosta, Ga., State Headquarters Selective Service, Atlanta, Ga.
PALMER, Clarence B., 1st Lieut., Covington, Ga.
PREAS, William G., Captain, Johnson City, Tenn.
ROBERTS, Louis C., 1st Lieut., Durham, N. C., Camp Peay, Tullahoma, Tenn.
SAMS, Frank H., 1st Lieut., Reynolds, Ga.
SAUNDERS, Joseph H., 1st Lieut., New Orleans, Meridian, Miss.
SELIGMAN, Ewing, Captain, Nashville, Tenn., Camp Shelby, Miss.
SIMS, Murphy M., 1st Lieut., Oxford, Miss., Camp Blanding, Fla.
SMITH, Phillip D., 1st Lieut., Knoxville, Tenn., Camp Shelby, Miss.
STATON, Leon R., 1st Lieut., Hayesville, N. C.
STOVALL, James T., Jr., 1st Lieut., Jefferson, Ga.
STROHMENGER, Frank J., 1st Lieut., Kingsport, Tenn.
SULLIVAN, Francis M., 1st Lieut., Atlanta, Ga., Fort Benning, Ga.
THARP, George W., Jr., 1st Lieut., Knoxville, Tenn., Fort McClellan, Ala.
WEINER, Harry, Captain, Birmingham, Ala., Camp Peay, Tullahoma, Tenn.
WEINSTEIN, Alfred A., Captain, Atlanta, Ga.
WYLIE, Paul E., 1st Lieut., Bemis, Tenn., Camp Peay, Tullahoma, Tenn.

YOUNG, John J., 1st Lieut., Natchitoches, La., Camp Shelby, Miss.
YUCKMAN, William, 1st Lieut., Quitman, Ga., Savannah A. A. Firing
Center, Savannah, Ga.
ZIEMAN, Alphonse H., 1st Lieut., Mobile, Ala., Camp Beauregard, La.

Orders Revoked

Orders have been revoked on the following named officers reported in previous report:

CARNEY, Henry M., Captain, Nashville, Tenn., Savannah A. A. Firing
Center, Savannah, Ga.
CRAIGHEAD, Claude C., 1st Lieut., Athens, La., Camp Blanding, Fla.
McCLARY, George R., 1st Lieut., Miami, Fla., Camp Peay, Tenn.

RAY, Emmett B., 1st Lieut., Kosciusko, Miss.
WEBB, John K., 1st Lieut., Columbia, S. C., 4th Division, Fort Benning,
Ga.
WILLIEN, Leon J., Captain, Knoxville, Tenn.

Orders Changed

Changes have been made in the station or effective date of orders in the following named officers:

PHILLIPS, James R., 1st Lieut., Baton Rouge, La., Camp Beauregard, La.
SCOTT, Wood H., 1st Lieut., Bonita, La., Fort McClellan, Ala.
WARSHAUER, Samuel E., 1st Lieut., Wilmington, N. C., Camp Shelby,
Miss.

FIFTH CORPS AREA

The following medical reserve corps officers had been ordered to active duty by the Fifth Corps Area Order up to and including midnight, November 8. The Fifth Corps Area comprises the states of Ohio, Indiana, Kentucky and West Virginia:

ALLEN, Chester H., Captain, Portsmouth, Ohio.
ARCHER, Maurice C., 1st Lieut., Medina, Ohio.
AYERS, Lloyd R., Captain, Beckley, W. Va.
BARNHART, John W., 1st Lieut., Clendenin, W. Va.
BAUHOF, Ned F., 1st Lieut., Canton, Ohio.
BEDINGER, Francis E., 1st Lieut., Walton, Ky.
BLOOMER, Richard S., 1st Lieut., Rockville, Ind.
BONNELL, George H., Jr., 1st Lieut., Worthington, Ohio.
BOOHER, Norman R., 1st Lieut., Indianapolis.
BOWSHIER, Robert E., 1st Lieut., Toledo, Ohio.
CARSON, James H., Captain, Martins Ferry, Ohio.
COLBERT, Morgan R., 1st Lieut., Louisville, Ky.
CONRAD, Harold A., Captain, Elkins, W. Va.
CELLIO, Lewis W., Captain, Carrollton, Ohio.
CRANSTON, Clyde J., Captain, Wakeman, Huron County, Ohio.
DAVIDSON, William D., Captain, Evansville, Ind.
DIETL, Ernest L., 1st Lieut., South Bend, Ind.
DILLARD, Harry K., 1st Lieut., Ashland, Ky.
DORROH, Glenn U., Captain, Columbus, Ohio.
DURKEE, Melvin S., 1st Lieut., Evansville, Ind.
EISNER, David G., 1st Lieut., Cleveland.
EVERETT, Clyde W., Captain, Cleveland.
FORD, Sylvester C., 1st Lieut., Cleveland.
GEIGER, Franklin R., 1st Lieut., Cincinnati.
GILLESPIE, Benjamin S., 1st Lieut., Tacoma, Ohio.
GITLIN, William A., 1st Lieut., Bluffton, Ind.
GRAU, Harry R., Captain, Cleveland.
GROVE, Thomas L., 1st Lieut., Huntington, W. Va.
HEWLETT, Thomas H., 1st Lieut., New Albany, Ind.
HOOVER, Reuben B., 1st Lieut., Columbus, Ohio.
KANNER, Irving F., 1st Lieut., Lexington, Ky.
KAPLAN, Ronald R., 1st Lieut., Cleveland Heights, Ohio.

KAUFFMAN, Nelson N., 1st Lieut., Indianapolis.
KILMER, John H., 1st Lieut., Fort Wayne, Ind.
LACOCK, Walter B., Captain, Columbus, Ohio.
LAMONICA, Leon L., 1st Lieut., Cleveland.
LEICHLITER, John W., Captain, Cincinnati.
LIPSCOMB, William N., Major, Lexington, Ky.
LOEB, William J., 1st Lieut., Cleveland Heights, Ohio.
LUND, Leonard C., 1st Lieut., Argos, Ind.
LYBROOK, William B., 1st Lieut., Galveston, Ind.
LYONS, Robert E., Jr., Captain, Bloomington, Ind.
LYTLE, Robert P., Captain, Cleveland.
MARCHANT, Clarence H., 1st Lieut., Bloomington, Ind.
MARCUS, Louis L., 1st Lieut., Toledo, Ohio.
MATSON, John W., 1st Lieut., Uhrichsville, Ohio.
McEWEN, James W., Captain, Terre Haute, Ind.
McLAUGHLIN, Calvin P., 1st Lieut., Pendleton, Ind.
MEILING, Richard L., 1st Lieut., Columbus, Ohio.
MISHKIN, Irving, Captain, Elkhart, Ind.
MOORE, Kenneth G., Captain, Fort Worth, Texas.
NORTHUP, Clarence E., II, 1st Lieut., Columbus, Ohio.
NOVACK, Benjamin F., 1st Lieut., East Chicago, Ind.
PEACOCK, Norman F., 1st Lieut., Crawfordsville, Ind.
PEASE, Phillip P., Captain, Chardon, Ohio.
PEBWORTH, James T., 1st Lieut., Indianapolis.
PICKAR, Daniel N., 1st Lieut., Wheeling, W. Va.
ROBBINS, James S., 1st Lieut., Mayfield, Ky.
RODENBERG, Elmer J., Captain, Columbus, Ohio.
ROUSH, Carl E., 1st Lieut., Cincinnati.
SHARP, John L., 1st Lieut., Crawfordsville, Ind.
STANLEY, John S., 1st Lieut., East Chicago, Ind.
STOREY, William R., 1st Lieut., Hobart, Ind.
TEMPLETON, Ames R., 1st Lieut., South Bend, Ind.
THOMAS, Morris C., Captain, Indianapolis.
THOMPSON, Roy H., Captain, Cleveland.
TOUPKIN, Jerome H., 1st Lieut., Charleston, W. Va.
WAGENAAR, Edward H., Captain, Shipshewana, Ind.
WELCH, Brent A., 1st Lieut., Sidney, Ohio.
WIER, James A., 1st Lieut., Evansville, Ind.
WILSON, Orley E., 1st Lieut., Elkhart, Ind.

SIXTH CORPS AREA

The following additional medical reserve corps officers had been ordered to extended active duty by Sixth Corps Area Order up to November 22. The Sixth Corps Area comprises the states of Wisconsin, Illinois and Michigan.

ASKWIG, LeRoy C., 1st Lieut., Detroit.
BENNETT, Keith F., Captain, Kalamazoo, Mich.
BENNETT, Sanford A., 1st Lieut., Detroit.
DANA, Harold M., 1st Lieut., Detroit.
FITZGERALD, Maurice D., Captain, Chicago.
GAYNES, Harvey E., 1st Lieut., Chicago.
GOLDIN, Morris I., 1st Lieut., Detroit.

GORDON, Harold L., 1st Lieut., Detroit.
GREENBERG, Morris Z., 1st Lieut., Detroit.
HAUSER, Maurice J., 1st Lieut., Chicago.
HIRSCHFELD, Alexander H., 1st Lieut., Ann Arbor, Mich.
JULIAR, Benjamin, 1st Lieut., Detroit.
KENNEDY, Donald J., 1st Lieut., Detroit.
KOON, William D., 1st Lieut., Grand Rapids, Mich.
LARIMORE, Granville W., 1st Lieut., Chicago.
LASSAR, Gilbert N., 1st Lieut., Springfield.
MALLER, Adolph M., 1st Lieut., Chicago.
QUARTON, Albert E., Jr., 1st Lieut., Ann Arbor, Mich.
RYGH, Edgar A., Captain, Highland Park, Ill.
SHINGLMAN, Willard E., Captain, Cicero, Ill.
SUGARMAN, Marcus H., 1st Lieut., Detroit.
WARNKE, Robert D., 1st Lieut., Detroit.

NINTH CORPS AREA

Following are the names of medical reserve corps officers ordered to extended active duty by Ninth Corps Area Order for the week ended November 16. The Ninth Corps Area comprises the states of Washington, Montana, Wyoming, Oregon, Nevada, Utah, California and Idaho.

BANKS, Gerald F., 1st Lieut., San Diego, Calif., Presidio of Monterey,
Calif.
BARNES, Norman J., 1st Lieut., Los Angeles, Fort MacArthur, Calif.
COZEN, Lewis N., Captain, Los Angeles, Fort Lewis, Wash.
DAVIS, Irving, Captain, San Francisco, Presidio of Monterey, Calif.
DONICH, George M., 1st Lieut., Butte, Mont., Fort Lewis, Wash.
GARDNER, Elsworth L., 1st Lieut., Eugene, Ore., Fort McDowell, Calif.
GOERKE, Lenor S., 1st Lieut., Woodland, Calif., With State Director
of Selective Service, State of California.
GROSSBLAT, Jacob, 1st Lieut., Los Angeles, Presidio of Monterey,
Calif.

HOORWITZ, Emanuel, Captain, Alcatraz Island, Calif., Fort McDowell,
Calif.
HUDSON, Charles B., 1st Lieut., Oakland, Calif., Presidio of Monterey,
Calif.
KELTZ, Charles, 1st Lieut., Los Angeles, Presidio of Monterey, Calif.
MASON, James L., Captain, Los Angeles, Presidio of Monterey, Calif.
MITCHELL, Charles S., 1st Lieut., Fresno, Calif., Presidio of Monterey,
Calif.
NAGEL, Sherman A., Jr., 1st Lieut., Los Angeles, Presidio of Monterey,
Calif.
NEUGARTEN, Kurt, 1st Lieut., San Francisco, Presidio of Monterey,
Calif.
PALMER, Alfred M., 1st Lieut., San Francisco, Fort Lewis, Wash.
SCHENK, Harry Leon, 1st Lieut., Los Angeles, Presidio of Monterey,
Calif.
SLAUGHTER, Howard C., Major, Los Angeles, Presidio of Monterey,
Calif.
SPEAKER, Otho F., 1st Lieut., Glendale, Calif., Fort MacArthur, Calif.

Orders Revoked
STRANQUSIT, Henry C., Major, Ogden, Utah.

ORGANIZATION SECTION

OFFICIAL NOTES

THE CLEVELAND SESSION

Section Representatives to Scientific Exhibit

Representatives to the Scientific Exhibit have been appointed from the different sections of the Scientific Assembly as follows:

- Practice of Medicine—Louis B. LaPlace, 1900 Rittenhouse Square, Philadelphia.
Surgery, General and Abdominal—Grover C. Penberthy, 1553 Woodward Avenue, Detroit.
Obstetrics and Gynecology—H. Close Hesseltine, 5841 Maryland Avenue, Chicago.
Ophthalmology—Georgiana Dvorak Theobald, 120 Medical Arts Building, Oak Park, Ill.
Laryngology, Otology and Rhinology—Fred W. Dixon, 2060 East Ninth Street, Cleveland.
Pediatrics—Arthur F. Abt, 104 South Michigan Avenue, Chicago.
Pharmacology and Therapeutics—O. P. J. Falk, 539 North Grand Boulevard, St. Louis.
Pathology and Physiology—F. W. Konzelmann, Temple University Hospital, Philadelphia.
Nervous and Mental Diseases—F. P. Moersch, 102 Second Avenue, S.W., Rochester, Minn.
Dermatology and Syphilology—Hamilton Montgomery, 102 Second Avenue, S.W., Rochester, Minn.
Preventive and Industrial Medicine and Public Health—Paul A. Davis, 1436 Delia Avenue, Akron, Ohio.
Urology—John H. Morrissey, 40 East Sixty-First Street, New York.
Orthopedic Surgery—Theodore A. Willis, 10515 Carnegie Avenue, Cleveland.
Gastro-Enterology and Proctology—Sara M. Jordan, 605 Commonwealth Avenue, Boston.
Radiology—S. W. Donaldson, 326 North Ingalls Street, Ann Arbor, Mich.
Anesthesiology—Paul M. Wood, 745 Fifth Avenue, New York.

Application blanks for space in the Scientific Exhibit at the Cleveland session may be obtained from the section representatives or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

American Medical Golfing Association

In 1913 Dr. Will Walter first suggested the founding of a medical golfing association to Dr. Wendell Phillips, then a trustee of the American Medical Association, who responded with an enthusiasm which continued until his death in 1934. The organization work, which fell to Dr. Walter, was completed in time for the initial tournament, which was held at the San Francisco Country Club in 1915. A tournament has been held by the golfing association during the time of the annual session of the American Medical Association each year since 1915. Following is a list of the tournaments, where they were held, the champion, and the president and vice president:

The average attendance of players at the tournaments has been about 210. Their popularity has increased until it has become necessary to select a country club which has two eighteen hole courses or to take over two courses which are adjacent to each other, as was done in Kansas City in 1936 and as will be done in Cleveland in 1941. The present membership of the golfing association is 1,610 fellows in all parts of the United States, Hawaii, Cuba and the Philippine Islands.

The 1941 tournament of the American Medical Golfing Association will be held at the Cleveland Country Club and Pepper Pike in Cleveland during the annual meeting of the American Medical Association in that city, June 2-6. This year's president of the American Medical Golfing Association, Dr. E. H. Houston of Seattle, has had a long golfing career. He has been president and captain of the largest municipal links in Seattle and a member of its board of trustees for fifteen years, and president of the golfing section of the Washington State Medical Association for the last sixteen years. He was chairman of the greens committee of one club for twenty-five consecutive years. The physicians of British Columbia and King County Medical Society, Washington, for twenty-two years have had an annual golfing tournament, and Dr. Houston has been president of the King County group. He has regularly attended the tournaments of the American Medical Golfing Association for years and already he has completed all arrangements for the next tournament of the American Medical Golfing Association.

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the American Medical Association meeting at Cleveland on June 3, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the programs at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and

Tournament	Year	Club	Champion	President	Vice President
First	1915	San Francisco Country Club	James Eaves	Wendell Phillips*	Will Walter
Second	1916	Detroit Country Club	Fred Bailey	Wendell Phillips*	Will Walter
Third	1917	Garden City Golf Club, New York	A. F. Henning	Thomas Hubbard	Will Walter
Fourth	1918	Glenview Club, Chicago	F. M. Caster	Fred Bailey	Will Walter
Fifth	1919	Atlantic City Country Club	Fred	Martin	Will Walter
Sixth	1920	New Orleans Country Club	A. F.	Marvel*	Will Walter
Seventh	1921	Common Country Club, Boston	Charlt	Moss	Will Walter
Eighth	1922	Glen Echo Club, St. Louis	Fred Bailey	Charlton Wallace	Will Walter
Ninth	1923	San Francisco Country Club	E. Seaforth	Will Walter	Fred Bailey
Tenth	1924	Olympia Fields, Chicago	George McKee	James Eaves	Fred Bailey
Eleventh	1925	Seaview, Atlantic City	Homer Nicoll	D. Chester Brown	Lorenzo Walter
Twelfth	1926	Dallas Country Club	S. M. Hill	Henry Cotton*	Walt Conaway
Thirteenth	1927	Columbia Country Club, Washington	George McKee	Samuel Childs	Leland Ellis
Fourteenth	1928	Minneapolis Country Club	Walter Sheldon	W. D. Shelden	H. H. Kerr
Fifteenth	1929	Waverly Country Club, Portland	John Loudon	Ben Thomas*	G. J. Thomas
Sixteenth	1930	Hawthorne Country Club, Detroit	John Loudon	Walter Schaller	J. L. McCool
Seventeenth	1931	Aronimink Country Club, Philadelphia	George McKee	Edwin Zabriskie	Frank A. Kelly
Eighteenth	1932	New Orleans Country Club	S. M. Hill	Frank A. Kelly	John Welsh Croskey
Nineteenth	1933	Blue Mound Country Club, Milwaukee	Mark Bach	John W. Croskey	J. P. O'Kelley
Twentieth	1934	Mayfield Country Club, Cleveland	John Loudon	Homer K. Nicoll	J. W. Powers
Twenty-first	1935	Northfield Country Club, Atlantic City	L. C. Foster	Charles Lukens	John B. Morgan
Twenty-second	1936	Mission Hills and Kansas City Country Club	Roy E. Emanuel	M. M. Cullom	Walt P. Conaway
Twenty-third	1936	Seaview Country Club, Atlantic City	W. J. VanWie	W. Albert Cook	Clarence Capell
Twenty-fourth	1938	San Francisco Golf and Country Club	J. A. Marek	Walt P. Conaway	George W. Hall
Twenty-fifth	1939	Norwood Hills Country Club, St. Louis	Duke R. Gaskins	E. S. Edgerton	James W. Morgan
Twenty-sixth	1940	Winged Foot Golf Club, Mamaronek, New York	John M. Murphy	George W. Hall	Grayson Carrell

*Deceased

broadcast it at another hour or even on another day. It is advisable therefore to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles

will be announced weekly in THE JOURNAL and monthly in *Hygeia*, the Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

- December 4. Paging Dr. Drew.
- December 11. The Family's First Friend.
- December 18. A Stitch in Time.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. Res. 630 has passed the House, providing that an additional assistant in the attending physician's office of the House of Representatives shall be paid the sum of \$30 a month from the contingent fund of the House until otherwise provided for by law. H. R. 10278 has passed the House and Senate, providing that until May 15, 1945, the Secretary of War may, in his discretion, dispense with any part of the examination for promotion in the Regular Army of officers of the Medical, Dental and Veterinary Corps, except those relating to physical examination. During the course of the consideration of this bill on the floor of the House, Repre-

sentative Crawford, of Michigan, proposed that original appointments in the Medical Corps of the Army "shall be made from among graduates of reputable schools or colleges of medicine or osteopathy, under such regulations as the Secretary of War shall prescribe." The amendment was not adopted.

DISTRICT OF COLUMBIA

Changes in Status.—H. R. 8665 has been reported to the Senate, providing for the issuance of a license to practice chiropractic in the District of Columbia to Lou Davis. H. R. 10418 has been reported to the Senate, authorizing the Commission on Licensure to issue a license to practice the healing art in the District of Columbia to Dr. Peter Florey.

WOMAN'S AUXILIARY

Georgia

The Mrs. James N. Brawner cup was won last year by the Woman's Auxiliary to the Ware County Medical Society at Waycross and the previous year by the auxiliary to the Baldwin County Medical Society at Milledgeville. Mrs. Brawner, of Atlanta, first president of the Woman's Auxiliary to the Medical Association of Georgia, presented the cup to the auxiliary for award at each annual meeting, the winner to retain possession until the following meeting. Mrs. Eustace A. Allen, of Atlanta, is chairman of the trophy committee and has compiled the list of credits that will govern the award of the cup this year. A yearbook will be stressed, health education programs, subscriptions to *Hygeia*, the payment of dues on time and an exhibit at the state meeting.

An auxiliary to the Gwinnett County Medical Society was organized at a meeting in Lawrenceville. Mrs. C. W. Roberts, of Atlanta, former president of the Woman's Auxiliary to the Medical Association of Georgia, was the chairman of organization. Mrs. D. C. Kelley, of Lawrenceville, was named president of the new group.

The Woman's Auxiliary to the Randolph County Medical Society met recently with Mrs. J. C. Patterson in Cuthbert.

Illinois

The Aux Plaines branch of the Cook County auxiliary met, September 27, in Oak Park with the president, Mrs. C. W. Stuart, presiding. One hundred and two members and guests were present. Among the honored guests were Mrs. H. J. Dooley, state president; Mrs. W. C. Bornemeier, county president; Mrs. R. K. Packard, past national president, and Mrs. W. J. Wanninger, national *hygeia* chairman.

The north side branch of the Cook County auxiliary met, September 16, at the McCormick Y. W. C. A., Chicago, with twenty-one members and three guest speakers present. The program was "Information Please." Mrs. R. K. Packard spoke on "Why an Auxiliary?" Mrs. C. G. Goodwin, parliamentarian of the Illinois Federation of Women's Clubs, on parliamentary procedure, and Dr. W. O. Thompson, secretary to the north side branch of the Chicago Medical Society, gave a short address and answered questions.

The Central Branch of the Woman's Auxiliary to the Cook County Medical Society met, October 2, at the Medical-Dental Arts Building, Chicago, with fifty members and guests present. Mrs. W. C. Bornemeier introduced the two guest speakers, Dr. Frank Maple, president of the Chicago Medical Society, and Mrs. H. J. Dooley, president of the state auxiliary. Both spoke on "The Aims and Objectives of the Auxiliary."

The St. Clair County auxiliary met, October 3, in the auditorium of St. Mary's Hospital, East St. Louis, with twenty-eight members present. The president, Mrs. O. M. McCann, presided. The speakers were Mrs. Ethelynn Sullivan, executive secretary of the St. Clair County Tuberculosis Association, and Dr. C. Milton Eberhart, district health superintendent of district number 16. Mrs. W. A. Griffith gave a report on legislative news and Mrs. I. L. Foulon reviewed *Hygeia*. Mrs. R. B. Ellis, radio chairman, presented "The Care of the Skin" on Station WTMU, October 7.

Wisconsin

The twelfth annual meeting of the state auxiliary was held in Milwaukee, September 17-19, with 354 members registered.

Mrs. V. E. Holcombe, president of the Woman's Auxiliary to the American Medical Association, was guest of honor. Three other national board members were present: Mrs. Robert Fitzgerald, chairman of revisions; Mrs. Eben J. Carey, a director, and Mrs. George H. Ewell, chairman of press and publicity.

The honorable Carl F. Zeidler, mayor of the city of Milwaukee, a guest speaker, commended the woman's auxiliary for its work in the field of improvement of public health and described the organization as a front line of defense for the ideals of American medicine. He predicted that in the coming legislative session many measures not in the interest of the health of Wisconsin citizenry would again be introduced, and he encouraged the studying of legislative bills and the dissemination of authentic information on them.

Mrs. Frank W. Pope is the retiring president, Mrs. Donne F. Gosin the president for 1940-1941 and Mrs. J. S. Supernaw the president-elect.

At the annual dinner Dr. Eben J. Carey, dean of Marquette University School of Medicine, gave an address.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 1931.

CALIFORNIA

The Clinical Aspects of Dermatology.—The University of California Medical School, San Francisco, has announced plans for a refresher course on "Clinical Aspects of Dermatology," to be given in the University of California Hospital, January 6-8. The program will cover various common cutaneous conditions, including tumors. Surgical aspects of dermatology will be considered and there will be lectures on infectious diseases. Additional information may be obtained from the Dean's Office, University of California Medical School, Medical Center, San Francisco.

Society News.—The San Francisco County Medical Society devoted its meeting, October 8, to a symposium on "Can We Get Adequate Nursing Care?" The speakers were Dr. Russell V. Lee, Palo Alto, from the point of view of the general practitioner; Dr. Anthony J. J. Rourke, the hospital superintendent; Marjorie Hart, R.N., private duty nurse; Sally Heitman, R.N., nurses' training school, and Helen Reynolds, R.N., visiting nurse.—Mr. Arthur Cornelius Jr., director of the Los Angeles office of the Federal Bureau of Investigation, discussed "Present Day Problems of Law Enforcement, with Special Reference to Cooperation from the Medical Profession" before the Hollywood Academy of Medicine, October 10.

IDAHO

Life Membership in State Society.—Dr. Joseph N. Davis, Twin Falls, was presented with life membership in the Idaho State Medical Association, September 12, as a token of appreciation for many years of faithful and efficient service. Dr. Davis has attended every annual session of the state association since becoming a member in 1913. He served as secretary-treasurer from 1922 until 1931, when he was made president-elect. From 1935 to 1938 he was a councilor. He was elected secretary-treasurer again in 1938, serving until this year, when he asked to be relieved. He is now state chairman for the Committee on Medical Preparedness of the American Medical Association.

EDITORIAL NOTE.—As we go to press, news is received that Dr. Davis was killed in an automobile accident, November 6.

ILLINOIS

Postgraduate Conference.—The Madison County Medical Society will be host at a postgraduate conference arranged by the state medical society for physicians in the sixth district in Alton, December 4. The following program will be presented by Chicago physicians:

- Dr. Henry Close Hesselstine, Newer Endocrines in Obstetrics.
- Dr. Lowell D. Snorf, Diagnosis and Treatment of Functional Disorders of the Colon.
- Dr. Clifford J. Barborka, Medical Management of Gallbladder Disease.
- Dr. Wilber E. Post, Arthritis.
- Dr. Hillier L. Baker, Potential Inguinal Hernia with Special Reference to Direct Hernia.
- Dr. Archibald L. Hoyne, Scarlet Fever.
- Dr. Arno B. Luckhardt, Academic or Unsuccessful Research.
- Dr. Warren H. Cole, Hypertthyroidism.

Chicago

Public Lecture by Dr. Ebaugh.—Dr. Franklin G. Ebaugh, professor of psychiatry, University of Colorado School of Medicine, Denver, will address a public meeting sponsored by the Chicago Medical Society in cooperation with the Chicago Pediatric and Neurological societies, December 11, at the Chicago Woman's Club. His subject will be "Your Mental Health."

Branch Meetings.—Dr. John de J. Pemberton, Rochester, Minn., discussed "Indications for Splenectomy and the Results of Operation" before the North Side Branch of the Chicago Medical Society, November 7. Dr. Albert M. Snell, Rochester, addressed the Evanston Branch, November 7, on "Recent Studies on Deficiency States and Vitamin Therapy" and Dr. Charles B. Puestow, "Relation of Vitamins to Surgery."

Society News.—The Chicago Council of Medical Women was addressed, November 13, by Drs. Mila I. Pierce, Evanston, on "Infections of the Newborn"; Louise O. Kappes, Evanston, "Allergy in Children," and Willie Mae Clifton, "Dietary Treatment of Phosphorus Retention in Renal Insufficiency."—The Chicago Gynecological Society was addressed, November 15, among others, by Drs. Milton H. Adelman and Benjamin B. Lennon on "Pituitrin Shock."

IOWA

District Meeting.—The Iowa and Central Illinois District Medical Association held its winter meeting in Davenport, November 15. Dr. Rieber C. Hovde, Davenport, gave a "Statistical Analysis of 115 Consecutive Operations on the Biliary Tract" and Dr. Donald Guthrie, Sayre, Pa., "Diagnosis of Diseases of the Thyroid Gland and Their Treatment."

Annual Fracture Clinic.—The fourth annual "fracture day" sponsored by the fracture committee of the Iowa State Medical Society was held in Cedar Rapids, November 14, in conjunction with the meeting of the Linn County Medical Society. The session was devoted to a symposium on fractures of the spine with the following speakers: Drs. George L. Apfelbach, Chicago; Arthur Steindler, Frank R. Peterson and Clarence E. Van Epps, Iowa City; Arthur W. Erskine and Robert M. Wray, both of Cedar Rapids; Douglas N. Gibson, Lewis M. Overton and Francis A. Ely, Des Moines. The clinic was concluded with a lecture by Dr. Donald Guthrie, Sayre, Pa., on "Thyroid Disease." Dr. Guthrie was the guest speaker of the Linn County Medical Society.

MARYLAND

The Noguchi Lectures.—Dr. Heinrich Zimmer, formerly professor of Sanskrit at the University of Heidelberg, delivered the Hideyo Noguchi Lectures at the Institute of the History of Medicine, Johns Hopkins University School of Medicine, Baltimore. The general subject was "Hindu Medicine," presented in three parts:

- November 25, Medical Tradition and the Human Body.
- November 27, The Physician and His Concept of Dietetics.
- November 29, Diseases and Cures.

Professor Pearl Dies.—Raymond Pearl, Ph.D., professor of biology, Johns Hopkins University School of Medicine, Baltimore, died suddenly in Hershey, Pa., November 17, of coronary thrombosis, aged 61. Born in Farmington, N. H., June 3, 1879, Dr. Pearl graduated at Dartmouth College in 1899, where he also received an honorary degree in science in 1919. He received his degree in philosophy from the University of Michigan in 1902, an honorary doctorate in laws from the University of Maine in 1919 and one in letters from St. John's College, Annapolis, in 1935. Dr. Pearl began his career as assistant zoologist at Michigan in 1899, becoming instructor in 1902. In 1906 he went to the University of Pennsylvania for one year. From 1907 to 1918 he was biologist and head of the department of biology at the Experimental Station in Maine. He became professor of biometry and vital statistics at the Johns Hopkins University School of Hygiene and Public Health in 1918, serving as research professor from 1925 to 1930. He was named professor of biology in the school of medicine in 1923 and in the school of hygiene and public health in 1930, holding both positions until his death. He was director of the institute of biologic research at the school from 1925 to 1930. He was president of the International Union for Scientific Investigation of Population Problems from 1928 to 1931 and later of other scientific bodies. He wrote extensively on his subject.

MASSACHUSETTS

Society News.—Dr. Richard H. Overholt, Brookline, addressed the Trudeau Society of Boston, October 24, on "The Management of Pulmonary Abscess."—The Northeastern Conference on Mental Health was to be held in Salem, November 15; the speakers included Drs. Ira S. Wile, New York, "Mental Health of the Community," and Harry C. Solomon, Boston, "Diagnosis and Treatment of Mental Disorders."

Memorial Meeting to Dr. Maude Abbott.—The New England Heart Association held a special meeting at the Boston Medical Library, November 8, in honor of the late Dr. Maude E. S. Abbott, formerly assistant professor of medical research and curator of the medical museum, McGill University Faculty of Medicine, Montreal. The speakers were:

- Dr. Charles F. Martin, Montreal, Dr. Abbott and McGill University.
- Dr. Paul D. White, Boston, Her Contribution to Cardiology.
- Dr. Emanuel Libman, New York, Personal Reminiscences.
- Dr. Helen B. Taussig, Baltimore, Changes Which Occur During Life in Patients with Congenital Malformations of the Heart.

MINNESOTA

Personal.—Dr. Bertram S. Adams, Hibbing, president of the Minnesota State Medical Association, was honored at a dinner, October 22. Dr. Adams had been selected as the "seventh annual honor night choice" by the Hibbing Elks Lodge. —Dr. William F. Braasch, Rochester, was recently made a corresponding member of the Sociedad Venezolana de Urología and of the Sociedad Cubana de Urología.

Society News.—Dr. Walter Henry Valentine, Tracy, has been named president of the Southern Minnesota Medical Association and Dr. Nelson W. Barker, Rochester, reelected secretary-treasurer. —Dr. Julian F. DuBois, Sauk Centre, has been chosen president of the Northern Minnesota Medical Association and Dr. Clarence Jacobson, Chisholm, secretary. —Dr. William F. Braasch, Rochester, addressed the Minnesota Academy of Medicine, November 13, in St. Paul, on "Hypertension and Surgical Disease of the Kidney." Dr. William A. H. Hanson, Minneapolis, presented his thesis on "Tumors Simulating Carcinoma—Hand-Schüller-Christian's Disease."

NEW YORK

Society News.—Drs. Wardner D. Ayer and Abraham C. Silverman addressed the Onondaga County Medical Society, Syracuse, November 4, on "Chronic Cerebral Disease—A Critical Review with Special Reference to Diagnosis and Treatment" and "Outbreak of Poliomyelitis in a Child-Caring Institution in Syracuse" respectively. —At a meeting of the Syracuse Academy of Medicine, November 19, the speakers were Drs. Marguerite P. McCarthy, Solvay, and Joseph R. Wiseman on "An Analysis of Treated Hay Fever Patients at the Allergy Clinic, Syracuse Free Dispensary"; Frederick S. Wetherell, "Nodular (Adenomatous) Goiter—Present Day Concepts of Its Management," and Robert C. Schwartz, "Patent Ductus Arteriosus, with Operation—Case Report."

New York City

The Welch Lectures.—Dr. Francis Peyton Rous, member of the Rockefeller Institute for Medical Research, will deliver the William Henry Welch Lectures, presented by Mount Sinai Hospital, December 6 and 9. Dr. Rous's subjects will be "Conditions Determining Cancer" and "The Known Causes of Cancer."

Meeting on Chronic Pulmonary Diseases.—The Tuberculosis Sanatorium Conference of New York will hold a clinical session on chronic pulmonary diseases at Cornell University Medical College, December 11. The program will be presented by the staff of the Municipal Sanatorium, Otisville, as follows: Drs. Samuel A. Thompson, New York, and Mortimer Greenberg, Otisville, "A Plea for the Early Jacobaeus Operation in the Treatment of Incomplete Collapse Therapy"; Joseph Emerson Noll, Port Jervis, "Data Concerning Location and Measurements of Pulmonary Cavities and Foreign Bodies," and Milton S. Lloyd, "Pulmonary Drainage: Its Relation to Collapse Therapy in the Treatment of Tuberculosis."

Friday Afternoon Lectures at the Academy.—Dr. Irving S. Wright delivered the fourth Friday Afternoon Lecture of the current series at the New York Academy of Medicine, November 29, on "Thrombophlebitis—Recent Advances in Knowledge and Treatment." Coming lectures will be:

Dr. Ralph H. Boots, Gold Therapy in Rheumatoid Arthritis, December 6.

Dr. James William Hinton, Cancer of the Stomach: Early Diagnosis and Surgical Indications Based on the Review of 700 Cases, December 13.

Dr. Norman H. Plummer, Specific Treatment of Pneumonia, January 3. Dr. Tracy J. Putnam, The Nature and Treatment of Epilepsy, January 10.

Dr. John Scudder, Newer Knowledge of Blood Transfusion, January 17. Dr. Kenneth R. McAlpin, Blood Diseases from the Standpoint of the Clinician, January 24.

Previous lectures in the series were: Drs. Harold J. Stewart on "Digitalis Therapy: Mechanism of Its Action in Congestive Heart Failure," November 1; Harold T. Hyman, "Massive Dose Chemotherapy or Intravenous Drip Chemotherapy," November 8, and Thomas Duckett Jones, Boston, "Care of the Patient with Rheumatic Fever," November 15.

NORTH CAROLINA

Special Society Meetings.—Dr. Milton R. Gibson, Raleigh, was elected president of the North Carolina Eye, Ear, Nose and Throat Society at its annual meeting in Winston-Salem, recently. Dr. Thomas C. Kerns, Durham, was made vice president and Dr. Vanderbilt F. Couch, Winston-Salem,

secretary. Guest speakers at the meeting were Drs. William Thornwall Davis, Washington, D. C., on "Physiotherapy in Ophthalmology" and "Medical Ophthalmology" and Edward A. Looper, Baltimore, on "Cancer of the Larynx" and "Laryngeal Tuberculosis." The society voted to require that henceforth applicants for membership must have passed examinations of the American Board of Ophthalmology or the American Board of Otolaryngology. —Dr. Robert W. McKay, Charlotte, was elected president of the North Carolina Urological Association at the annual meeting in Greensboro, October 14. Dr. John W. Frazier Jr., Salisbury, was elected vice president and Dr. William C. Lott, Asheville, secretary. The guest speaker at the meeting was Dr. Roy B. Henline, New York, who spoke on "Adequate Treatment of Prostatic Disease from a Pathological Viewpoint."

PENNSYLVANIA

Easton Hospital Fifty Years Old.—The fiftieth anniversary of the founding of Easton Hospital, Easton, was observed November 11. Open house was held at the hospital and a plaque honoring the first board of trustees was unveiled. The hospital was established in 1890 with a fund of \$7,000 raised by a hospital bazaar, said to have been the most important social event in the town's history. The first building, a remodeled residence, had ten beds. Additions were made in 1894 and a new brick building replaced the early frame structure in 1906. The present building, with facilities for 192 patients and twenty-one newborn infants, was built in 1930.

Philadelphia

The DeSchweinitz Lecture.—Dr. Frederick H. Verhoeff, Boston, delivered the third annual DeSchweinitz Lecture before the section of ophthalmology of the College of Physicians of Philadelphia, November 20. His subject was "Occlusion Hypertropia."

Anthrax and Industry.—The bureau of industrial hygiene of the Pennsylvania Department of Health and the Philadelphia Department of Health sponsored a symposium on anthrax, November 19, at the Philadelphia County Medical Society Building. The speakers were:

Col. Arthur Parker Hitchens, History and Biology of the Anthrax Bacillus.

Dr. Pascal F. Lucchesi, Treatment of Anthrax.

Dr. Henry Field Smyth, Anthrax in the United States.

Ivor Griffith, Ph.M., The Felt Hat Industry.

Harry D. Immel, Pennsylvania Department of Labor and Industry, The Enforcement Problem.

Dr. William B. Fulton, Joseph F. Meller Jr. and William H. Kreeker Jr., bureau of industrial hygiene, state health department, Harrisburg, An Anthrax in Philadelphia.

L. B. F. Raycroft, Industrial Hygiene Association, Helpful Relationships for Prevention of Anthrax.

Pittsburgh

Society News.—Speakers at a meeting of the Pittsburgh Academy of Medicine, November 12, were Drs. Bender Z. Cashman on "The Role of Deep Cauterization in the Prevention of Cancer of the Cervix"; Charles Russell Schaefer, Pittsburgh, "Glycolysis in Leukemia," and William A. Heazlett, Wilkinsburg, "Masked Diabetes Insipidus." —Drs. James H. Rankin Jr. and Michael Cammarata, Woodville, addressed the Pittsburgh Neuropsychiatric Society, November 18, on "Fracture Prevention in Metrazol Treatment; Demonstration of Technic" and "Treatment of Epilepsy, with Special Reference to Dilantin" respectively.

VIRGINIA

Portrait of Dr. Tucker.—Ex-residents of Tucker Sanatorium, Richmond, presented a portrait of Dr. Beverly R. Tucker to the sanatorium recently. Dr. Thomas G. Hardy, Farmville, made the presentation for the ex-residents and Dr. Howard R. Masters accepted for the sanatorium. Dr. James Asa Shield presided at the exercises, which were attended by a number of ex-residents now practicing in other cities.

Regional Meetings.—The Southwestern Virginia Medical Society met at the Southwestern State Hospital in Marion, October 2, with Drs. Russell L. Haden, Cleveland, and David C. Wilson, Charlottesville, as the guest speakers on "Treatment of Anemia" and "New Drugs in Neuropsychiatry" respectively. —The Clinch Valley Medical Society held a meeting at Norton, October 18, with the following speakers: Drs. James T. Tucker, Richmond, on "The Use of Modern Drugs in Traumatic and Orthopedic Surgery"; Henry C. Spalding, Richmond, "Practice of Obstetrics in the Home"; Fred J. Wampler, Richmond, "Progress in the Prevention of

Diseases"; George Fordham, Powellton, W. Va., "Developing a Medical Program for a Coal Industry," and Mr. R. T. Homewood of the state health department, who outlined the part that the bureau of industrial hygiene may play in a health program for the mining industry.

WASHINGTON

Society News.—The fall meeting of the Pacific Northwest Dermatological Society was held in Spokane, October 17. Dr. Hamilton Montgomery, Rochester, Minn., was the guest speaker on "Pathology of Skin Diseases."—Speakers before the King County Medical Society, Seattle, November 4, were Drs. Philipp Schonwald, on "Fungus Allergies"; James E. S. Stroh, "Treatment of the Acute Asthmatic Patient," and Alexander R. Altose, "The Allergic Nose." All are of Seattle.—Dr. Joseph A. Beeman, Portland, Ore., addressed the Spokane County Medical Society, Spokane, November 14, on "The Role of the Medical Profession in Criminal Investigation."

GENERAL

Conviction of Norman Baker Sustained.—On November 22 the conviction of Norman Baker and his two associates R. A. Bellows and Dr. J. L. Statler, on a charge of using the mails to defraud, was affirmed by the Eighth Circuit Court of Appeals at St. Louis. In January 1940 Baker was sentenced by the Federal District Court to four years in prison and fined \$4,000 in connection with the promotion of his cure for cancer.

Venereal Disease Rates in Cities and States.—The U. S. Public Health Service has issued a statement on the prevalence of syphilis and gonorrhea in cities for the fiscal year 1940; some of the rates for cities, however, are based on fewer than twelve months. A statement has also been issued giving the rates for these diseases by states. The total annual rate for syphilis per thousand of population was 3.68 and varied for the various states from 0.37 for Wisconsin to as much as 20.34 for Mississippi. The syphilis rate for the Virgin Islands was 20.09, Florida 13.94, District of Columbia 10.76 and South Carolina 10.27. The annual rate per thousand of population for gonorrhea totaled 1.36, varying from 0.40 for Wisconsin to 14.39 for Mississippi. The gonorrhea rate for the Virgin Islands was 9, District of Columbia 5.36, Alaska 3.92 and Arizona 3.28. The data on which these reports were based were monthly reports from state and city departments of health. The total number of new cases of syphilis reported by states for the month of August 1940 was 38,088, and of new cases of gonorrhea 15,921. The new syphilis cases reported included primary, secondary, early latent and congenital cases.

Academy of Dermatology and Syphilology.—The third annual meeting of the American Academy of Dermatology and Syphilology will be held at the Palmer House, Chicago, December 8-11. The preliminary program announces that there will be special courses, luncheon round table discussions, clinical presentations, lectures and symposiums. Courses in histopathology and mycology and the clinical presentations will be at the University of Illinois College of Medicine. Among subjects of the symposiums will be: physiology and chemistry of the skin, led by Dr. Donald M. Pillsbury, Philadelphia; pharmaceutical therapeutics, by Dr. Otto H. Foerster, Milwaukee; allergy, by Dr. Samuel M. Peck, New York, and syphilis, by Dr. Udo J. Wile, Ann Arbor, Mich. Addresses will be given by the following:

- Dr. Cyrus C. Sturgis, Ann Arbor, Mich., Diseases of the Blood and Blood Forming Organs: Their Relation to the Skin and Mucous Membranes.
- Dr. Edward A. Oliver, Chicago, Rare Dermatoses.
- Dr. Lyle B. Kingery, Portland, Ore., Recent Advances in Our Knowledge of the Ringworm Infections.
- Dr. Elmer L. Sevringhaus, Madison, Wis., Endocrines and Their Relation to Dermatology.
- Dr. William F. Petersen, Chicago, The Patient, His Skin and the Weather.

Annual Meeting of Infantile Paralysis Foundation.—The National Foundation for Infantile Paralysis held its first annual medical meeting, November 7-8, at the Waldorf-Astoria Hotel, New York. Reports were heard from the committees on virus research, public health (epidemics), research for the prevention and treatment of after-effects, education, medical publications and nutritional research. The committees recommended grants totaling \$150,580 for the coming year, including one of \$6,600 for epidemic aid in the Philippine Islands. Dr. Herman N. Bundesen, Chicago, was elected chairman of the committee on public health (epidemics) to succeed Dr. Thomas Parran, surgeon general. U. S. Public Health Service, Wash-

ington, D. C., who resigned because of the pressure of other activities. Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, was elected chairman of the committee on medical publications to succeed Dr. Max M. Peet, Ann Arbor, Mich. The following chairmen were reelected: Drs. Thomas M. Rivers, New York, committee on virus research; Philip Lewin, Chicago, committee on research for prevention and treatment of after-effects; James S. McLester, Birmingham, Ala., committee on nutritional research, and Dr. Peet, committee on education. At a banquet Thursday evening Mr. Basil O'Connor, New York, president of the foundation, delivered the principal address. The dinner was attended by 120 persons, including committee members, trustees and officers, forty-four grantees of previous years and newspaper science editors and writers.

National Institute of Health Studies Problems of Aging.—A new unit formed in the National Institute of Health for the study of problems of aging, called the Unit on Gerontology, announces that it is conducting a survey of the present trends of active and contemplated investigations in this field. Inquiries about studies on aging are being sent to scientists in the basic biologic sciences as well as to clinical investigators, in the belief that much fundamental work on the processes, mechanisms and consequences of senescence is going on in sciences related to medicine. Critical analysis of the information elicited by such a survey may be expected to serve several purposes, the announcement said. It should facilitate closer cooperation among investigators interested in related problems and it will emphasize the urgent need for augmented support of studies for the problems of senescence. It will reveal "blank spots" in research that may justify special emphasis in the future and will be an invaluable aid in formulating future research programs, it was said. Dr. Edward J. Stieglitz, Garrett Park, Md., is in charge of the investigations in gerontology, and the following national advisory committee has been appointed:

- Dr. Lewis R. Thompson, director, National Institute of Health, Washington, D. C.
- Dr. Anton J. Carlson, Frank P. Hixon distinguished service professor emeritus of physiology, University of Chicago.
- Dr. Charles L. Christiernin, New York, medical director, Metropolitan Life Insurance Company.
- Robert E. Coker, Ph.D., professor of zoology, University of North Carolina, Chapel Hill, N. C.
- William Crocker, Ph.D., director, Boyce Thompson Institute of Plant Research, Yonkers, N. Y.
- Mr. Lawrence K. Frank, sociologist, Josiah Macy Jr. Foundation, New York.
- Albert Baird Hastings, Ph.D., Hamilton Kuhn professor of biological chemistry, Harvard University, Cambridge, Mass.
- Dr. Ludvig Hektoen, Chicago, consultant, National Cancer Institute, U. S. Public Health Service.
- Dr. Winfred Overholser, superintendent, St. Elizabeths Hospital, Washington, D. C.
- Dr. Clarence D. Selby, medical consultant, General Motors Corporation, Detroit.
- Dr. William D. Stroud, professor of cardiology, The Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

A conference of this committee was held at the institute, November 25-26. Information concerning subjects under investigation and the methods of approach is earnestly solicited. Letters should be addressed to Dr. Stieglitz, In Charge, Investigations in Gerontology, National Institute of Health, Bethesda, Md.

FOREIGN

Physicians in the New Germany.—According to the *Münchener medizinische Wochenschrift*, Germany now has (in the region of the old reich) 59,454 physicians, compared to 55,259 during 1937. During the latter year Germany still had 4,220 Jewish physicians. In the "Ostmark" (Austria) the estimated number of physicians is 7,000, in the Sudeten district 2,000. If the numerous approbations during last year are counted in, the total number of physicians may be estimated at approximately 75,000. Three Japanese women physicians have arrived in Berlin for a half-year's stay in Germany. In Japan two of them were active in gynecologic clinics and one in the department for infants in a Red Cross hospital. Their studies in women's occupations, social work and medicine will be made under the patronage of the "Reichsfrauenführung" (women's organization of the reich) and of the "Reichsärzteführer" (leader of the physicians of the reich). Japan has at present 5,500 women physicians. By a decree of the Rumanian minister of health, thirty-four Jewish physicians who were active as county physicians were dismissed; the dismissal was effective immediately. Likewise thirty-one Jewish physicians connected with the social insurance were removed from their positions.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 2, 1940.

Medical Education Under the Air Raids

London has twelve medical schools, without counting post-graduate ones, the greatest number in any city in the world. The continuous bombing has damaged many of the hospitals to which they are attached as well as school buildings. But medical education is not interrupted, though it goes on in a different way. London was divided into sectors with the great hospitals at the apexes and connected to affiliated hospitals in the surrounding country, to which most of their patients were removed, so that they could be used as casualty clearing stations for the victims of air raids, who were expected to number many thousands. Thanks to our defenses and air raid precautions the number has been much smaller. The students were dispersed to the "sector hospitals." It was hoped to resume normal teaching at the London hospitals on the opening of this winter session. But the bombing, which has seriously damaged some of them, has prevented this. St. Thomas's Hospital received three direct hits from bombs in six days and had to be evacuated. Though the foundation of the hospital goes back to medieval times, the present building, with its eight linked pavilions and medical school on the bank of the Thames, is one of the most modern of the London hospitals. It has been necessary to make arrangements for the preclinical teaching in the country as well as for the clinical teaching at sector hospitals. The London hospital has been hit several times but the walls have not been damaged and there have been no casualties. However, the precaution has been taken of reducing the number of beds, and now only acutely ill patients and casualties are admitted. But systematic teaching continues at the hospital, though clinical work is done by the students at the sector hospitals in the mornings. They return in the afternoons to the hospital for the systematic teaching. One new advantage is that, while in peace time only 800 beds were available at the London Hospital, the sector hospitals provide 10,000. Similar arrangements are made by the other schools. The preclinical students are sent to medical schools in other cities, some as distant as Bristol and Cardiff, or to improvised schools in the country. While the material for the clinical students is much diminished at their own hospitals, they have the advantage of a much greater number of beds at the sector hospitals. Hence the remark of one dean that their education, though less academic, is more practical. The preclinical students of St. Bartholomew's Hospital are housed in the University Laboratories [censor]. Those of Guy's Hospital are receiving their tuition at temporary premises in [censor], those of University College Hospital at the [censor] National School [censor].

The Growing of Medicinal Plants

Few medicinal plants are grown in this country; we have to rely on imports, which the war has interrupted. The Ministry of Health, in collaboration with the Ministry of Agriculture, is taking measures to secure an adequate home supply of the four important plants belladonna, hyoscyamus, stramonium and digitalis. At the same time work is being done along genetic and ecologic lines to increase the yield of active principles from these plants. The Therapeutic Requirements Committee of the Medical Research Council has also recommended the production or collection of numbers of medicinal plants in Britain, such as colchicum, filix mas, hamamelis, pyrethrum. Bulletins on the growing of these plants are issued by the Ministry of Agriculture. More has not been done in this direction in the past because the plants could be imported at prices which would not

pay for their growing at home. It is also suggested by the Therapeutic Requirements Committee that more drugs should be grown in the British Empire, which can produce every important drug. Among the examples given are camphor, cascara sagrada, cinchona, coca, ipecacuanha, turpentine, santolin, thymol. It has been stated by J. C. Ghosh in his book "Indigenous Drugs of India" that half the drugs of vegetable origin in the British pharmacopeia are indigenous to India and that nearly all the others could be grown there.

The War Strain on Health Services

In Parliament the minister of health, Mr. Malcolm MacDonald, stated that the war had thrown a strain on our health services which they had successfully withstood. Because of the dangers of air raids, 730,000 children and 420,000 mothers were evacuated from industrial cities to the country. This huge migration was from populous areas where the necessary medical services were well established to areas where they were sparse. The difficult problem presented to the health authorities had to be met by swift improvisation. A skilled staff was recruited, and houses and other buildings were transformed into sick bays, residential nurseries, residencies for cripples and maternity homes. For London mothers alone homes were furnished in the country to cope with 2,800 confinements every month, and 500 expectant mothers were now leaving London every week. The evacuation of that much bombed city and of other cities was not a prelude to defeat nor the death agony of Britain but rather the unpleasant, the terrible but hopeful birth pangs of a new Britain. A fact about the new Britain was that the sojourn of London and other city children in the country had made them taller, heavier and more resistant to illness.

THE EMERGENCY HOSPITAL SERVICE

The Emergency Hospital Service was a remarkable creation. To the great resources of our hospitals had been added other public institutions, which by provision of operating rooms and equipment were transformed into first class hospitals. The permanent hospitals had been surrounded by new pavilions which could hold tens of thousands of extra patients. The number of air raid casualties was small compared with the efforts of the German airmen. At the moment only 5,500 beds had air raid casualties. Among the problems aggravated by the war was venereal disease. Its incidence had shown a large and steady decline in the past twenty years, but in the last few months there were indications of an increase. Local authorities were being asked to expand the existing services where necessary.

Precautions Against Disease in Air Raid Shelters

In a broadcast, Mr. Malcolm MacDonald, minister of health, spoke of the dangers to national health from overcrowding of air raid shelters in the coming winter and the arrangements to combat possible epidemics which might result. The most potent threat might be not the bomb and the parachute but the germs of influenza and other infectious diseases which generally can be held in check in peace time. The toughest new problem had been created by the gathering of people to sleep night after night in the large air raid shelters. Infectious diseases might lodge there and spread. The danger would be much reduced if the nightly population of the shelters was kept within reasonable proportions. Apart from influenza the dangerous disease most likely to spread to the camps and shelters this winter was cerebrospinal fever. But sulfapyridine had reduced the mortality of that disease to a fraction of what it was. Among the precautions to be taken was the setting up of medical aid posts in the large centers. There would be a nurse in regular attendance and a physician either in residence or on call. The shelters would be equipped to minister not only in cases of accident but for minor ailments which might be aggravated by the life in them.

In connection with the government's scheme to supply medicine for minor ailments in public shelters, it is proposed to set up local pharmacists' rotas for personal service. The War Emergency Council of the Pharmaceutical Society is discussing this development with the Ministry of Health. The stocks at these miniature underground pharmacies would be limited to a small range of preparations for immediate use by persons showing symptoms of nasal catarrh, throat and lung troubles or other ailments of an infectious nature. There would be an adequate supply of gauze pads to apply to the nose and mouth of persons with symptoms suggesting the presence of germs. These pads would be a signal to others to keep at a distance. Antiseptic compounds and surgical dressings would also be kept in readiness.

In the eighty stations of the London underground railways, 100,000 persons find shelter from bombs. They sleep on the platforms and passages in perfect safety. The latest arrangement is to distribute to them, by a special train, tea, coffee and cocoa, supplied at a charge of 2 cents per cup, and light refreshments, such as buns, biscuits, apples and sausage rolls, for which the maximum charge is 4 cents. The London County Council is providing 7,000 hot meals daily at its community centers for persons whose dwellings have been destroyed by bombs.

Criticism of the War Loaf

Nutritional experts have been stressing the superiority of bread made with wholemeal flour over that made with white flour because the latter is deficient in important ingredients, particularly vitamin B₁ and minerals. In spite of this, white bread remains much more popular than wholemeal. The government, which now controls and rations our food supply, has decided to fortify white bread by the addition of vitamin B₁ and calcium. This step was taken after receiving the report of a scientific committee. The decision has given rise to much controversy in the *Lancet*. In announcing this war bread in the House of Commons the minister of food described the drawbacks of wholemeal bread as unpalatability, indigestibility, lack of keeping qualities of white flour and invincible preference of the community for white bread. Sir Ernest Graham-Little, dermatologist and member of Parliament, points out that the report of a committee of the Royal Society on the digestibility of bread furnishes a direct negative to these allegations. Why did not the Ministry of Food follow the measures adopted in the last war on the advice of the committee of the Royal Society, one of which was the supply of a wholemeal war loaf? The measure now adopted involves the extraction from wheat of the major part of its vitamin content and the restoration of only vitamin B₁ in synthetic form. Graham-Little claims that the natural vitamin is superior to the synthetic. He also suggests that commercial interests are opposed to the loss of their trade in the by-products of the milling of white flour. A biochemist, R. A. Peters, contradicts Graham-Little as to the superiority of the natural vitamin and states that the synthetic vitamin is shown by every test—chemical, physical, biologic and clinical—to be equivalent. A cardiologist, Isaac Harris, is concerned about the addition of calcium to the bread. In his book "High Blood Pressure" he has shown that the kidney is exposed to a considerable strain when called on to excrete an excess of calcium and that a moderate administration has a profound influence on the character of the electrocardiogram.

The American Hospital Unit

The arrival of the American hospital unit, led by Dr. Philip Wilson, professor of orthopedic surgery at Columbia University College of Physicians and Surgeons, has been reported in previous letters. After landing at Liverpool the unit spent a week in visiting hospitals in the northwest under the guidance of Prof. Harry Platt of Manchester. It then came to London, where it was welcomed by the Ministry of Health and other

official bodies. After a survey, it was decided that it should take over a section of the war hospital at Park Prewitt, which in normal times is a mental hospital of 1,450 beds. General surgery is done there, but no orthopedic center existed and it is proposed that the American unit shall develop this. At the same time employment will be found in the department established in the hospital by Sir Harold Gillies for the member of the unit specializing in facial and maxillary surgery. But the idea of a separate American hospital has not been dropped. If the war becomes more intense and casualties increase, the unit reinforced from the United States will proceed to this work. Professor Wilson has cabled to America with a view to forming a neurosurgical team, which is desired by the British Emergency Medical Service. It would be accompanied by its own x-ray and laboratory technicians. In addition to clinical work Professor Wilson desires to carry out some research and he has been in touch with the British Medical Research Council so as to link up with it anything he may do in this direction.

A Physician Who Became an Anthropologist

The death at the age of 67 of C. G. Seligman, F.R.C.P., F.R.S., emeritus professor of ethnology in the University of London, has removed a man who began a distinguished career in the medical profession and abandoned it to become an eminent anthropologist. Seligman received his medical education at St. Thomas's Hospital, where he had a research scholarship under the pathologist S. G. Shattock. He was invited to join the Cambridge Anthropological Expedition, led by A. C. Haddon to the Torres Straits and Borneo. With Rivers, McDougall and Myers he began anthropological work on a tribe in North Queensland. He studied native diseases and collected information on native magic and customs. Returning to England he was appointed director of the clinical laboratory at St. Thomas's Hospital. But the attraction of anthropology proved too great and he embarked on an expedition which resulted in a monumental work, "The Melanesians of New Guinea." Returning to England again he worked at pathology for the last time, contributing to the Proceedings of the Royal Society a paper entitled "Observations on the Acquirement of Secondary Sexual Characters Indicating the Formation of an Internal Secretion of the Testicle." In 1908 he was commissioned by the government of India to work on the Veddas, a primitive people of Ceylon. The book that resulted was produced in collaboration with his wife and remains a standard work on the history and culture of these people. They also studied African ethnology and produced "The Pagan Tribes of the Nilotic Sudan," which was the first complete cultural survey of these people. In 1910 he was appointed lecturer on ethnology in the University of London and in 1913 professor. He applied psychoanalysis to the folklore and dreams of primitive people and endeavored to trace freudian phases in their sexual life.

Marriages

WILLIAM C. KEETTEL JR. to Miss Mary Helen Shinn, both of Iowa City, at Waverly, June 30.

RAYMOND A. NEWTON, Genoa, Neb., to Mrs. Helen Carstens of Chicago in Omaha, June 29.

KENNETH L. McSHANE to Miss Della Jacobson, both of Loveland, Colo., June 28.

CLARENCE F. BANTIN to Miss Angeline Phillips, both of Omaha, July 14.

GORDON MARTIN to Miss Neva Cocklin, both of Lincoln, Neb., June 14.

LOUIS R. NASH to Mrs. Madeline Carey, both of Ingleside, Neb., July 6.

Deaths

Charles Edward Humiston ☉ Chicago; College of Physicians and Surgeons of Chicago, 1896; an Affiliate Fellow of the American Medical Association; member of the House of Delegates of the American Medical Association, 1915, 1916, 1918, 1919 and from 1921 to the special session of 1935; a member of the Council on Medical Education and Hospitals of the American Medical Association from 1930 to 1937; past president of the Illinois State Medical Society; past president and secretary of the Chicago Medical Society; professor of surgery emeritus at his alma mater, now known as the University of Illinois College of Medicine; formerly on the staffs of the Chicago State Hospital and the Cook County Hospital; in 1922 was awarded the honorary degree of doctor of science from Marietta (Ohio) College; aged 72; co-founder, president of the West Suburban Hospital Association, from 1911 to 1914; member of the board of directors and trustee and for many years on the staff of the West Suburban Hospital, Oak Park, where he died, November 4, of encephalomalacia, cerebral thrombosis and arteriosclerosis.

Quitman Underwood Newell ☉ St. Louis; University of Alabama School of Medicine, 1911; assistant, instructor, assistant professor, associate professor from 1915 to 1935 and professor of clinical obstetrics and gynecology at the Washington University School of Medicine; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Southern Surgical Association and the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; president-elect of the Southern Medical Association; served during the World War; associate obstetrician and gynecologist, Barnes, St. Louis Maternity and St. Louis Children's hospitals; obstetrician and gynecologist, St. Luke's and Missouri Baptist hospitals; aged 54; died, November 4, of coronary sclerosis.

Arthur Carroll Scott ☉ Temple, Texas; Bellevue Hospital Medical College, New York, 1886; member of the House of Delegates of the American Medical Association, 1911, 1924, 1925, 1926, 1927; member and past president of the Southern Surgical Association; past president of the State Medical Association of Texas, Central Texas Medical Society and the Texas Association of Railway Surgeons; fellow and member of the board of governors of the American College of Surgeons; formerly member of the state prison board; chief surgeon, Gulf, Colorado and Santa Fe Hospital; founder and president on the staff of the Scott and White Hospital; aged 75; died, October 27, of coronary occlusion.

Pascal Brooke Bland ☉ Philadelphia; Jefferson Medical College of Philadelphia, 1901; assistant professor of gynecology at his alma mater from 1915 to 1925 and professor of obstetrics from 1925 to 1937, when he was made professor emeritus; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; fellow of the American College of Surgeons; past president of the Obstetrical Society of Philadelphia; consulting obstetrician to the Jefferson Hospital; author of "Gynecology, Medical and Surgical" and "Obstetrics for Students and Practitioners"; aged 65; died, October 31, in the Bryn Mawr (Pa.) Hospital of a self-inflicted bullet wound.

William Henry Holmes ☉ Chicago; Northwestern University Medical School, Chicago, 1910; professor of medicine at his alma mater; member of the Central Society for Clinical Research; served during the World War; on the staffs of the Wesley Memorial Hospital and the Passavant Memorial Hospital; author of a book entitled "Infectious Diseases"; aged 53; died, November 2, in Ann Arbor, Mich., of pulmonary and cerebral abscesses.

George Dorsey Green, Lock Haven, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; member of the Medical Society of the State of Pennsylvania; past president of the Clinton County Medical Society; served during the World War; on the staff of the Lock Haven Hospital; aged 66; died, October 15, in the University of Pennsylvania Hospital, Philadelphia, of carcinoma of the pancreas.

John Joseph Maria Carey, Brooklyn; Long Island College Hospital, Brooklyn, 1908; member of the Medical Society of the State of New York; aide to Governor Lehman and formerly aide to President Franklin D. Roosevelt when he served as governor of New York; on the staffs of the Norwegian and Victory Memorial hospitals; served during the World War; aged 58; died, October 1.

Edward Everett Hicks, Brooklyn; University of the City of New York Medical Department, 1893; formerly assistant

clinical professor of neurology at the Long Island College of Medicine; member of the American Psychiatric Association; on the staff of the Kings County Hospital and the Brooklyn State Hospital; aged 69; died, October 18, of cerebral hemorrhage and arteriosclerosis.

Julius Burson Cooper ☉ Birmingham, Ala.; Chattanooga (Tenn.) Medical College, 1904; veteran of the Spanish-American War; was trustee of the Snead Junior College and Wesleyan College; on the courtesy staff of the Norwood Hospital and of the South Highlands Infirmary; aged 63; died, October 19, in the Veterans Administration Facility, Hines, Ill., of carcinoma of the pancreas.

Arthur Lynn Anderson, Springfield, Mo.; University Medical College of Kansas City, Mo., 1900; fellow of the American College of Physicians; served during the World War; on the staffs of St. John's Hospital, Burge Hospital and Springfield Baptist Hospital, Springfield, and the Missouri State Sanatorium, Mount Vernon; aged 65; died, October 25, of cerebral hemorrhage.

Edward John Lawrence, Spokane, Wash.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1908; member of the Washington State Medical Association; served during the World War; formerly member of the school board; on the staffs of the Sacred Heart, Deaconess and St. Luke's hospitals; aged 57; died, September 13, of acute coronary thrombosis.

Walter Harry Hassed, Lusk, Wyo.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1908; member of the Wyoming State Medical Society; formerly secretary and state health officer, Wyoming State Board of Health, and secretary of the state board of medical examiners; aged 56; died, September 23, of a self-inflicted gunshot wound.

Edward Clement Davidson, La Fayette, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1891; member of the Indiana State Medical Association; fellow of the American College of Surgeons; for many years county coroner; on the staffs of St. Elizabeth's and Lafayette Home hospitals; aged 73; died, October 7.

Lane Bruce Kline, Houston, Texas; George Washington University School of Medicine, Washington, D. C., 1907; formerly a medical missionary; served during the World War; formerly health officer; at one time with the Veterans Administration; aged 59; died, September 30, in the St. Joseph Hospital of heart disease.

Herbert Mott Bentley, Sterling, Kan.; Hahnemann Medical College and Hospital, Chicago, 1897; served during the World War; was a member of the board of education; formerly mayor and vice president of the state board of health; aged 68; died, August 28, in Lawrence of cerebral hemorrhage and arteriosclerosis.

Rudolf Freimuth Teschan, Milwaukee; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; during the World War served as a medical examiner; formerly on the staff of the Evangelical Deaconess Hospital; aged 63; died, October 7, of coronary heart disease.

Frank Albert Davis, Hampton, N. H.; Boston University School of Medicine, 1898; member of the Massachusetts Medical Society; served during the World War; formerly associated with the Veterans Administration; aged 74; died, October 8, in Washington, D. C., of acute cardiac dilatation and chronic myocarditis.

Francois Louis Hughes ☉ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1898; fellow of the American College of Surgeons; served during the World War; on the staff of the Women's Homeopathic Hospital; aged 62; died, October 14, in the Hahnemann Hospital of coronary thrombosis.

Ralph Carleton ☉ Springfield, Mass.; Harvard Medical School, Boston, 1894; member of the American Academy of Ophthalmology and Otolaryngology and the New England Ophthalmological Society; on the staff of the Springfield Hospital; aged 70; died, October 26, of coronary thrombosis.

Howard Meng Lanham, Marshall, Texas; Jefferson Medical College of Philadelphia, 1896; member of the State Medical Association of Texas; served during the World War; aged 66; died, October 7, in the Veterans Administration Facility, Gulfport, Miss., of arteriosclerotic heart disease.

Clermont E. Park ☉ Parkersburg, W. Va.; College of Physicians and Surgeons, Baltimore, 1905; veteran of the Spanish-American and World wars; on the staffs of the Camden-Clark Memorial Hospital and St. Joseph Hospital; aged 69; died, October 10, of chronic myocarditis.

John Ross Smith Martin ☉ Philadelphia; University of Maryland School of Medicine, Baltimore, 1904; served during the World War; aged 58; for many years on the staff of the Graduate Hospital of the University of Pennsylvania, where he died, October 9, of carcinoma of the colon.

Henry Anthony Baker, Kansas City, Mo.; University of California Medical Department, San Francisco, 1891; member of the Missouri State Medical Association; medical director of the Kansas City Life Insurance Company; aged 70; died, September 17, of acute coronary thrombosis.

George E. Denny, Madison, Ind.; University of Louisville (Ky.) Medical Department, 1893; member of the Indiana State Medical Association; formerly superintendent of the Muscatatuck Colony for feeble-minded; at one time member of the state legislature; aged 70; died, October 29.

Fred Paul Weltner, Charleston, W. Va.; College of Physicians and Surgeons, Baltimore, 1915; member of the West Virginia State Medical Association; served during the World War; aged 51; died, August 15, of coronary thrombosis, diabetes mellitus and fracture of the left arm.

Edward Bogard ☉ Outwood, Ky.; Barnes Medical College, St. Louis, 1904; member of the Washington State Medical Association; served during the World War; on the staff of the Veterans Administration Facility; aged 60; died, October 28, in Louisville of coronary occlusion.

Solomon Simmons Barnett, New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1886; member of the Medical Society of the State of New York; aged 77; died, October 30, in St. Luke's Hospital of carcinoma of the bladder.

Herbert Eugene Simrell, Clarks Summit, Pa.; Medico-Chirurgical College of Philadelphia, 1906; served during the World War; aged 59; died, September 28, in the Veterans Administration Facility, New York, of arteriosclerotic heart disease and prostatic abscess.

Herbert Windham Hewitt ☉ Detroit; Detroit College of Medicine, 1903; formerly assistant clinical professor of surgery at his alma mater; fellow of the American College of Surgeons; on the staff of the Grace Hospital; aged 65; died in October of coronary thrombosis.

Arthur Francis Barrett ☉ Jersey City, N. J.; Long Island College Hospital, Brooklyn, 1919; aged 46; formerly on the staff of the Margaret Hague Maternity Hospital and St. Francis Hospital, where he died, October 13, of hypertensive cardiovascular disease.

Robert George Cavanagh ☉ Muskegon, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1885; for many years on the staffs of the Hackley and Mercy hospitals; aged 82; died, October 29, of chronic myocarditis and arteriosclerosis.

Fred Browne Grosvenor, Columbus, Ohio; University of Michigan Homeopathic Medical School, Ann Arbor, 1911; served during the World War; aged 55; died, October 9, in the Veterans Administration Facility, Wood, of arteriosclerotic heart disease.

Hiram Jackson Clark ☉ Excelsior Springs, Mo.; Washington University School of Medicine, St. Louis, 1907; past president of the Clay County Medical Society; formerly member of the city council; aged 72; died, October 2, of coronary heart disease.

Lucy Winchell Pine, Washington C. H., Ohio; Laura Memorial Woman's Medical College, Cincinnati, 1897; member of the Ohio State Medical Association; aged 75; died, October 6, in the Harding Sanitarium, Worthington, of cerebral arteriosclerosis.

William H. Kunsman, Morrisville, Pa.; Jefferson Medical College of Philadelphia, 1884; for many years justice of the peace and county coroner; aged 81; died, October 6, in the Mercer Hospital, Trenton, N. J., of cerebral hemorrhage.

John Bennett Jr., Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1898; aged 72; died, October 6, in the Presbyterian Hospital of hypertension, cerebral embolus and hypertrophy of the prostate.

Samuel Sidney Foss, Jeffersonville, Ind.; University of Louisville (Ky.) Medical Department, 1886; member of the Indiana State Medical Association; served during the World War; aged 76; died, October 5, of heart disease.

Victor B. Parowski, Detroit; Loyola University School of Medicine, Chicago, 1918; served during the World War; aged 47; died, October 1, in the Mercy Hospital, San Diego, of pulmonary, laryngeal and intestinal tuberculosis.

Charles Cecil Barr ☉ Tilden, Neb.; Sioux City (Iowa) College of Medicine, 1907; fellow of the American College of Surgeons; medical director and owner of the Tilden Hospital; aged 56; died, September 29, of heart disease.

Alfred Oliver Gery, East Greenville, Pa.; Jefferson Medical College of Philadelphia, 1893; member of the Medical Society of the State of Pennsylvania; aged 75; was killed, October 12, when struck by an automobile.

John Ashby McElwain, Schenectady, N. Y.; Albany Medical College, 1911; member of the Medical Society of the State of New York; served during the World War; aged 55; died, October 6, of coronary sclerosis.

Gilbert Emmings Eddy, Heidelberg, Miss.; University of Alabama School of Medicine, 1907; member of the Mississippi State Medical Association; formerly mayor of Heidelberg; aged 56; died, October 5, of uremia.

Henry Edward Parry, Los Angeles; Hahnemann Medical College and Hospital of Philadelphia, 1893; served during the World War; on the staff of the Veterans Administration Facility; aged 69; died, August 27.

Robert Herschel Geer, El Paso, Texas; University of Texas School of Medicine, Galveston, 1913; member of the State Medical Association of Texas; aged 54; died, October 10, of carcinoma of the liver.

Louis Disler, Canandaigua, N. Y.; St. Louis University School of Medicine, 1936; on the staff of the Veterans Administration Facility; aged 28; died, October 8, following an operation for appendicitis.

Fred Puleston, Daytona Beach, Fla.; State University of Iowa College of Medicine, Iowa City, 1901; member of the Florida Medical Association; aged 75; died, October 7, of cerebral thrombosis.

Alexander Park Boag ☉ Clearfield, Pa.; Temple University School of Medicine, Philadelphia, 1934; aged 32; on the adjunct staff of the Clearfield Hospital, where he died, October 4, of neuronitis.

Lauris Blake Baldwin, Los Angeles; Northwestern University Medical School, Chicago, 1894; veteran of the Spanish-American and World wars; aged 70; died, October 6, of chronic myocarditis.

John Newton Campbell, Varnville, S. C.; Medical College of the State of South Carolina, Charleston, 1908; aged 62; died, October 15, in the Tri-County Hospital, Orangeburg, of coronary thrombosis.

Martha Magdeline Schaplowsky, Worcester, Mass.; University of Kansas School of Medicine, Kansas City, 1937; aged 40; died, September 14, in Denver of acute myelogenous leukemia.

Cassius H. Fullinwider, Mount Vernon, Ind.; Medical College of Ohio, Cincinnati, 1883; member of the Indiana State Medical Association; aged 86; died, October 11, of arteriosclerosis.

Louis Coblin, Anchorage, Ky.; Miami Medical College, Cincinnati, 1876; aged 88; died, October 2, in the Norton Memorial Infirmary, Louisville, of a fractured hip received in a fall.

John Marcus Koelle, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1901; aged 63; died, October 1, of chronic myocarditis.

George Middleton Irwin ☉ Lansdale, Pa.; Jefferson Medical College of Philadelphia, 1933; aged 33; died, October 9, at Bridgeport of tuberculosis.

Isaac Hollen Taylor, Springfield, Ill.; Rush Medical College, Chicago, 1871; aged 90; died, September 27, of coronary occlusion and arteriosclerosis.

Charles Birdsall Pearson, Anaheim, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1886; aged 77; died recently.

Effie C. Munro Paul, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1893; aged 70; died, September 30, of carcinoma.

Harold Eugene Sheldon ☉ Troy, N. H.; Boston University School of Medicine, 1936; aged 40; died, September 25, of carcinomatosis.

Charles J. Meyer, Denver; Kaiser-Wilhelms-Universität Medizinische Fakultät, Strassburg, Germany, 1874; aged 87; died, October 13, of cerebral hemorrhage.

Cicero F. Faulkner, Whitney, Texas; Louisville (Ky.) Medical College, 1898; aged 70; died, October 11, of carcinoma.

Bureau of Investigation

TWO "BUST DEVELOPERS" CEASE DEVELOPMENT

1. Curtis A. Davis and His Personal Collection of Fraud Orders

2. Gloria Mauro's "Firmform" Not so Firm

"Bust developers," whether in the form of mechanical devices, massage creams or internal treatments, have again and again been debarred from the mails by the Post Office Department. Though some promoters may have closed up shop, one notorious offender has repeatedly dodged the government's edicts against him.

The Davis-Cook Swindle

In this department of THE JOURNAL, March 5, 1938, appeared a discussion of the Post Office fraud order issued in July 1937, which debarred from the mails the Youth-Aid Products of Los Angeles. The article showed that this was a new name adopted by an old-time swindling outfit, the Jennie L. Cook Company, to circumvent a similar fraud order that had been issued against the same promoter in January 1936. The article further brought out the facts that the Curtis A. Davis who was the moving spirit in this concern had originally promoted other mail-order swindles from Chicago, that the first fraud order had been issued against him as long ago as August 1916, and that he had evaded it by changing most of the firm names under which he had been doing business, so that the Post Office found it necessary to issue a supplementary fraud order against him in January 1917 to cover these new names.

In time Davis transferred his nefarious activities to Los Angeles. According to the Post Office he once stated that he used the title "Jennie L. Cook Company" because Jennie L. Cook was the name of his sister, who lived next door to the rooming house from which he conducted his business, but he claimed she had no financial interest in the fraud. The Cook trade style was one he had long employed in his Chicago schemes.

In 1932 another government agency, the Federal Trade Commission, issued a Cease and Desist Order against Curtis A. Davis, trading as the Jennie L. Cook Co., Los Angeles. In this Curtis was ordered to (1) cease advertising as a woman; (2) cease implying in his advertising that the statements he made were from one woman to another; (3) cease claiming that the Jennie L. Cook Company was composed of Parisian beauty culturists; (4) cease advertising that the Cook "treatment" was scientific, was made from a French formula and was a constitutional vitalizer and a tissue builder; (5) cease claiming that by the use of the "treatment" a perfect figure could be developed and the human body could be properly proportioned, and (6) cease claiming that the "treatment" would fill up hollows in the body, give the user strength and remove wrinkles. The facts were briefly noted in this department of THE JOURNAL, April 30, 1932.

Considering Davis's record in quackery, it was hardly to be expected that he would regard this latest pronouncement from the government too seriously. Hence it is not surprising that his name bobbed up again in 1936 in a Post Office fraud order and in 1937 in another, which was later supplemented by still another fraud order. The fact is that the Federal Trade Commission itself was obliged to bring a second action against Davis, as the result of which it announced on Nov. 25, 1939, that it had got him to sign a stipulation promising to discontinue certain lies in his advertising. Among these were that his "Jane Cook's Wonder Tissue Creme" will furnish nourishment to the tissues or cells or increase the size of the bust, or that a flat chest is due to a lack of nourishment in the tissue cells of the chest or to the fact that in a case of flat chest the cells are shrunken or collapsed. Davis further agreed to cease representing that his product was in fact a "tissue" cream, either by using that word in the name of a product or otherwise. A New York concern which handled advertising for Davis also was prevailed on to promise similarly to withdraw these false claims for the nostrum.

But Davis, with the brazenness of a habitual law-breaker, continued to defy governmental restraints on his swindles. A new name, The Alvin Sales Co., entered the picture as Davis's latest

trade style. Again the Post Office made an investigation, which revealed that Davis's latest exploitation, the "Jane Cook Beauty Aids," included his old "bust developer" fraud, that the latter was now being put out as the "Jane Cook Method" and that it consisted of the "Wonder Tissue Creme" and "Wonder Tonic Tablets," these last for internal use. A government chemist testified that the cream was made up of wool fat, fatty oil, a minute amount of ash and 28 per cent of water and that each tablet contained 1 grain of ferrous carbonate with alkaloids, including brucine and strychnine amounting to about one-sixth grain of nux vomica. One tablet was to be taken twice daily and the cream was to be massaged on the breasts. As medical evidence introduced at the Post Office hearing showed that this combination treatment would produce practically none of the effects on the breasts claimed in Davis's advertising and that the preparations in question were practically identical with those named in previous fraud orders, a new one was issued against the names Curtis A. Davis, C. A. Davis, Jane Cook Method and Alvin Sales Co. on March 2, 1940, and postmasters were instructed to return to all senders when known (or when not known, to send to the Dead Letter Office) all letters addressed to the names given.

But soon afterward Davis again was found to be evading the fraud order, once more using a new name, "Mrs. J. Cook," under which title he continued to solicit prospective victims with literature on his "Wonder Tonic Tablets" and "Jane Cook's Massage Creme" for the development of the female figure. Hence on the recommendation of Judge Vincent M. Miles, Solicitor for the Post Office Department, on March 14, 1940, the recently issued fraud order was extended to cover the name of Mrs. J. Cook, Los Angeles.

Thus Davis and the Post Office seem to be engaged in one continuous bout of many rounds. Of course, there ought to be some way to terminate the necessity for such repetition of effort on the part of the Post Office Department in protecting the public. But since there apparently is no such mechanism, one can only hope that the postal authorities will not become disgusted or discouraged about the whole thing. After all this may help the unemployment situation at least as far as the Post Office Department is concerned. In these parlous times such accounts as this help to add to the gaiety of reflections on our government's legal activities.

The Gloria Mauro Fraud

Another "bust developer" swindle which emanates from Los Angeles was promoted as a "bust normalizer"—to build up underdeveloped breasts to normal size or to restore enlarged or sagging breasts to their former contour. This business was conducted by one John Frank Mauro operating under the names Gloria Mauro, Gloria Mauro Products and Gloria Mauro Company. It is reported that he started his scheme in Hollywood in December 1936 and also established an eastern sales agency in New York which eventually was discontinued. It appears that some time in 1937 Mauro, accompanied by his wife, went to Belgium and still resides there. Prior to going, it is said, he gave one Florence Whittle power of attorney to act as his legal representative and to continue the business in his absence.

The Post Office Department properly looked into Mauro's swindle and in a memorandum on the case Hon. W. E. Kelly, Acting Solicitor, brought out the foregoing facts and some others. He showed that neither Mauro nor Miss Whittle possessed any medical training or employed a physician or any one else possessing medical knowledge. The "treatment," a device known as the "Gloria Firmform," was described in the memorandum as follows:

The "Gloria Firmform," which costs the promoter \$3.50 to manufacture, is a metal, cup-shaped apparatus designed to fit over the breast. Attached to the top is a rubber hose to be connected with a water faucet. Water entering the device through the hose is expelled upon the base of, and about the breast in numerous, needle-like sprays. Leading from the apparatus is a metal outlet for water introduced therein by the hose. Directions for use sent with the device read in part as follows:

"The Gloria Firmform is ready for use when taken from the package. In using, simply attach the hose connector to any convenient cold water faucet. Press the Firmform snugly against the body, covering the breast, and with sufficient firmness to prevent water seepage around the rim. Turn on the water with the fullest force available. . . . The length of time required and the degree of success attained varies, of course, with the degree to which the breasts are underdeveloped, have sagged, aged, condition of health and size of

breasts. However, the tonic effect will be noticed quickly and two or three weeks' regular use of Firmform usually indicate the beginning of improvement that convinces the user that she should follow the directions faithfully until the bust fills, firms and assumes the contours so greatly desired by every woman.

"FOR DEVELOPMENT"

"The woman with flat, underdeveloped breasts, if in normal health, need not usually despair of ever being beautiful of form . . . of having the lovely, full, firm-pointed breasts that so few women have and yet so many could develop with the proper method and care."

The memorandum went on to show that, according to expert medical testimony in the case, the only effect which this device could produce if used according to the directions furnished would be a stimulation of the skin overlying the breasts through the action of the cold water, thus temporarily increasing the circulation of the blood in that region. This testimony showed, further, that the size, shape and contour of the female breasts depend on the amounts of fat and the glandular and fibrous tissues deposited within them. Hence the application of cold water by means of the "Gloria Firmform," even over a long period, would have no effect whatever on the physiologic factors that determine the amounts of these fatty and glandular tissues in the breasts. Further, fatty depositions in the breasts of these persons naturally would cause sagging or pendulous breasts and the mere application of cold water to the overlying skin of these organs could not correct their sagging.

Some of the expert medical testimony referred to in the memorandum aptly summarizes the worthlessness of such a treatment as follows:

" . . . in order to accomplish the promised results in both these types of cases, the temporarily increased flow of blood brought about by the cold water principle of the 'Gloria Firmform' would, in the one case, have to bring about an increased deposition of fat cells, and of glandular and fibrous tissues, and in the other, accomplish the diametrically opposite effect of removing the excess fatty and other deposits responsible for the sagging, pendulous condition. According to the medical evidence, neither the 'Gloria Firmform' nor any other single, uniform method of external treatment can operate to produce such opposing results."

The fraud order against Gloria Mauro, Gloria Mauro Company and Gloria Mauro Products was issued Nov. 3, 1939.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ARTIFICIAL LIGHTING AND WINDOWLESS BUILDINGS

To the Editor:—The National Defense Commission has many million dollars' worth of contracts pending for industrial buildings. In designing these the architects have attempted to make them of a "blackout" type. One way of doing this is to use windowless structures equipped completely with artificial light and air conditioning. Have you run across any industrial health reports, either from this country or from England, which would throw light on these questions: 1. Does the long time use of artificial light to the exclusion of natural light have any harmful effect on the eyes of workers? 2. Do windowless factories cause claustrophobia among workers? In case of an air raid would panic be more prevalent among workers in windowless buildings than in glazed buildings? (If there are any studies on claustrophobia among submarine crews, these might help answer this question.) 3. What effect does work in air conditioned windowless factories have on the sickness rate of employees? (We have seen some reports on health in air conditioned offices but don't recall any on health in air conditioned, windowless factories.)

W. G. Hazard, Toledo, Ohio.

ANSWER.—No one of these questions can be answered categorically and without recognition that many circumstances other than the exact ones mentioned influence the situation.

1. The long time use of artificial lighting to the exclusion of all natural light may have a harmful effect on the eyes of workers, but foremost because of the inadequacy or unsuitability of the artificial lighting provided. Until recently there has been no form of artificial lighting that compared favorably with daylight. Even now statements as to parity must be accepted with reserve. S. W. Fisher (*Lancet* 1:668 [April 6] 1940) compares the total incidence and incident rate of miners' nystagmus, which long has been England's foremost occupa-

tional disease, for the years 1930 to 1938 inclusive. In the first mentioned year, 3,066 new cases of miners' nystagmus appeared, constituting a rate per thousand of 4.15, while in 1938 the total number of new cases was 1,019, which provided a rate of 1.66. The only difference in work conditions has been the introduction of better illumination. The essence of this comment is that inadequate artificial illumination is the basis for nearly all unfavorable comparisons between natural and artificial lighting. In England, Patmore (*Indust. Welfare* 21:387, 1939), writing of efforts to meet the requirements of defense lighting, points out the necessity for high standards of illumination in order even to approach daylight and recommends high pressure mercury vapor lamps. This author notes that visual acuity is greater with this form of artificial illumination, in contrast to the tungsten lamp, in which it is stated that the maximum output is in the infra-red band, to which the visual apparatus of the eye is little responsive. The Industrial Health Research Board of England's Medical Research Council, in its first emergency report, entitled "Industrial Health in War," notes that some fine industrial work, particularly in persons with trivial eye defects, cannot be done with the best of lighting unless special optical aids are provided. Such operations call for industrial magnifiers, binoculars and at times the provision of corrective lenses for otherwise negligible deficiencies. It is now known from the work of Ferree and others (*Persomel Journal* 14:18 [May] 1935) that the illumination requirements for various age classes of persons are different. Thus a youthful group might attain a high level of acuity at 10 foot candles without any definite increase with augmented lighting. This is not true for workers of middle and early old age, whose lighting requirements are on a different level. With the advent of fluorescent lighting, with high intensity, absence of glare and a minimum of disturbing shadows, it is now possible to meet all the visual requirements of daylighting, but while artificial illumination may be made the equal or even the superior of daylight in selected enterprises, such as department store work, it should not be inferred that all the beneficent purposes served by sunlight are met.

2. Current comment on windowless air conditioned work places implies that such structures are radically new. Overlooked is the fact that most theaters are windowless, ventilated or air conditioned creations and that the counterpart of a windowless ventilated factory can be found in any mine. At this time every factory in Great Britain and other portions of the warring world has been made into a semiwindowless affair through the requirements of the blackout, much of which is described in the British Home Office Factory Department Publication entitled "Factory Ventilation in the Blackout." It is common experience that claustrophobia is not of common occurrence among theater patrons. On the other hand, few persons enter a mine or descend into a well without some anxiety. Claustrophobia is not a disease entity and certainly the mild apprehension which is the lot of most persons confronted with strikingly unusual physical surroundings cannot be regarded as significant. On moving into any new factory or office quarters of the windowless or opaque glass tile type of structure, fair numbers of all employees become more aware of air conditions, lighting and odors. In Detroit the Detroit Edison Company lately has constructed a large office building of highly modern design, completely air conditioned, with opaque glass tiles, permitting the entry of light but preventing any vision from within or without. During the early months after occupancy there arose many complaints from older women, and particularly scrub women working at night, protesting against being "put in a box." All such apprehension disappeared after a few months. In England this sort of situation has become associated with "gas obsessions." Owing to numerous breaks in gas lines there has been some warrant for anxiety on entering closed spaces. However, anxiety hysteria about gas dominates the picture. Usually these mild states are transitory and unimportant. When the anxiety is severe or prolonged, adequate inquiry ordinarily will establish causative connections wholly unrelated to physical surroundings. Among psychoanalysts the belief holds that all phobias, such as claustrophobia and agoraphobia, always represent an unconscious feeling of guilt resulting from an early disagreeable memory.

3. The intent of this comment is to recognize the possibility of a little "jumpiness" on the part of workers newly moved into windowless air conditioned work places but to deny the probability of creating any significant pathologic state by this type of architecture. When disturbing anxiety arises, fundamental causes should be sought in other places than windowless walls. See War Neuroses (London Letter, *THE JOURNAL*, Feb. 3, 1940, p. 424). In the case of submarine crews, the numerous excitants to anxiety preclude any possibility of segregating claustrophobia as an entity.

ALLERGIC SHOCK

To the Editor:—A man aged 37 of western Kansas was recently admitted to a local hospital complaining of numbness and tingling of the hands and feet and acute erythema, weakness, nausea and vomiting of about four hours' duration. The first attack was noted by the patient five years ago, during which he became dyspneic and cyanotic and fainted. He had severe substernal pressure with the first attack but has not had such a symptom since. He has about one or two attacks a year, usually in the spring and fall, and each attack is more or less typical. It begins with an erythema and a generalized sensation of warmth, which gradually increases and deepens to a maximum in anywhere from one-half hour to thirty-six hours. Attacks are always attended by severe bronchial secretion which is clear and contains no pus, also by nausea and vomiting. The present attack was the first in which he had numbness and tingling of the hands and feet. He has no pain during these attacks but usually has a slight headache for the following twenty-four hours. He is sick on the second day but is usually well and able to return to work by the third day. He has had chills and fever with each attack. He has had extensive laboratory studies and investigation from the standpoint of allergens, blood and urinalysis, gallbladder and gastrointestinal tract, x-ray and fluoroscopic studies, all of which have been normal. Extensive cutaneous tests were normal except for reaction to a few foods to which the patient showed sensitivity and which he has since avoided. When first seen by me the patient had an acute generalized erythema, his blood pressure was 60 systolic, 30 diastolic, and his pulse was rapid and thready. The skin, however, was hot and moist, and the patient was chilling vigorously and complained of being cold. He was given the supportive measures for shock and responded well, so that in about thirty minutes he felt much better and his nausea and vomiting had subsided to a mild degree. During the vomiting he regurgitated some undigested potato which he had eaten some ten hours previously. Urinalysis was not remarkable except for a heavy trace of albumin and numerous hyaline and granular casts. The white blood cell count was 13,550 with a normal differential. I suspected an allergic reaction, possibly a histamine-like reaction, as the cause of the condition, but I was not able to make a diagnosis and the patient states that his family physician has never arrived at a diagnosis. I should like to have an opinion as to the cause of this syndrome and would appreciate any suggestions you may have as to its treatment. M.D., Colorado.

ANSWER.—This interesting case offers a real diagnostic problem. The fall in blood pressure and other symptoms indicate the presence of some form of shock, although in shock fever and leukocytosis are not common. Since the attacks occur at long intervals and last only two or three days, and since there is complete freedom from symptoms between attacks, one is forced to conclude that there is no organic disease. Therefore the patient must have some nonorganic trouble or must be poisoned by some food. Food poisoning is possible although not likely.

A severe allergic reaction with shock is probably present. In favor of this diagnosis are (1) the severe bronchial secretion, (2) the erythema (pruritus is often associated), (3) the acuteness of the onset, (4) the relatively short duration and (5) the fall in blood pressure. Eosinophilia of the blood and sputum are usually present but are not necessary to make the diagnosis. Fever is uncommon, but can occur in severe allergic conditions.

Granted that the patient is allergic, it seems likely that the cause of the attacks is some substance to which the patient is exposed infrequently. This could be a food which he eats rarely or could be some inhalant, e. g. horse dander, dog hair, orris root (perfume) or perhaps a drug, such as acetylsalicylic acid, quinine or some hypnotic. Tests should be made both cutaneously and intracutaneously not only for the common antigens but also for the rare ones, e. g. karaya gum (wave set), Brazil nuts, mango and artichokes. Cutaneous tests for drugs are unsatisfactory. Instances of severe allergic shock to rare antigens are not uncommon and death has occurred occasionally from such substances as peanut butter, poppyseed, Brazil nuts, glue or some drug. The patient should keep a food record and should also record any unusual exposures to animals, drugs or the like. Epinephrine should be administered for any further attacks.

TONSILLECTOMY AND HEMORRHAGE PREVENTION

To the Editor:—I have told a family that outside of seeing that a child is in the best physical condition, and provided the coagulation time is normal, there is nothing to be given preoperatively to prevent bleeding in a tonsillectomy, should the technic be good. A relative's doctor has informed them that I was wrong. Consequently for the family's benefit I would appreciate it if you would reply to this question.

Sidney Schreiber, M.D., Forest Park, Ill.

ANSWER.—This question has been the subject of many discussions, conferences and literary contributions by laryngologists all over the world. The advice given is basically sound and is the method used by the majority of specialists. Indeed, many men do not even have the coagulation time taken unless the history warrants it. The essential points are a good history, physical examination and the drawing of inferences and conclusions as to the operative fitness and condition of the child.

If the history is such as to suggest an inquiry into the possibility of postoperative hemorrhage, then appropriate blood studies

should be made including coagulation, bleeding time and platelet count. Though such studies are important, it must be remembered that they are often not reliable, and too much attention should not be paid to them. Where the observations fall far below normal, certain precautions may be undertaken preoperatively. Parenteral injection of small amounts of horse serum or whole blood, or even larger amounts of blood by transfusion when anemia is also present, may be employed to shorten coagulation or bleeding time. Where serum is employed, allergic sensitivity must be ruled out, although the principle of sensitization to a foreign protein (requiring about ten days) has been suggested as a means to prevent the occurrence of hemorrhage in hemophilia by subsequent intradermal administration of the protein to increase the coagulability of the capillary blood. The intradermal injections do not desensitize the patient. In thrombocytopenic purpura, blood transfusion is an effective means of restoring the platelet count to normal or near normal. Even in hemophilia surgery can be safely undertaken if transfusions are given during the operation and healing period, to hold the coagulation time near normal. The use of blood or serum as prophylaxis against hemorrhage is probably more effective than the use of calcium salts, estrogens and placental or other tissue extracts. The Council on Pharmacy and Chemistry has not accepted for New and Nonofficial Remedies any of these preparations as effective prophylactic agents against hemorrhage, except nonimmune horse serum. Thromboplastic substances are recognized by the Council for local use in the treatment of hemorrhage from oozing surfaces, as is also the use of iron compounds for their styptic or astringent properties. The Council has deferred consideration of the use of snake venom as a parenteral hemostatic agent in the treatment of hemorrhagic conditions because of the meager evidence available. The experience recently reported concerning the effectiveness of Koagamin (a compound containing oxalic and other dicarboxylic acids derived from the plant shepard's purse) as a prophylactic parenteral coagulant is insufficient to warrant more than experimental use until further evidence becomes available. Some years ago the Council declared Styptsate, another proprietary hemostatic prepared from shepard's purse, not acceptable for New and Non-official Remedies.

Each case requires individual study, observation and evaluation and must be dealt with accordingly. There are a number of eminent laryngologists who hold exactly the same opinion that has been expressed by the inquirer.

DURATION OF POSITIVE BENZIDINE TEST AFTER GASTROINTESTINAL BLEEDING

To the Editor:—A question arose on ward rounds as to the duration of the positive guaiac or benzidine test on the stool after the cessation of active bleeding in the gastroduodenal region and elsewhere in the gastrointestinal tract. References would also be appreciated.

Victor F. Lief, M.D., Far Rockaway, N. Y.

ANSWER.—The figures given by various authors for the average duration of a positive benzidine test for occult blood in the stool following hemorrhage from a peptic ulcer are in general agreement. This period was 13.6 days in eighty cases recently reported by Turnbull and Sagi (*Am. J. Digest. Dis. & Nutrition* 6:92 [April] 1939). Meulengracht (*Lancet* 2:1220 [Nov. 30] 1935) found that an average of 13.4 days with 4.5 defecations elapsed before the stools were entirely negative with Gregersen's benzidine test on the "old form" of treatment of bleeding peptic ulcers and that an average of 10.2 days elapsed with 4.8 defecations when the Meulengracht treatment was employed. The latter group consisted of 251 cases. The difference of approximately three days in the duration of positive benzidine reactions was not taken as an indication of a shorter period of bleeding. Noth and Wilbur (*Proc. Staff Meet., Mayo Clin.* 10:824 [Dec. 26] 1935) found the average duration of a positive benzidine reaction in five cases to be ten and a half days from the time of admission. Presumably hospitalization was soon after the onset of hemorrhage. It should be noted that figures for average duration are not directly applicable to an individual case. Schiodt (*Am. J. M. Sc.* 193:313 [March] 1937) gives the average time as 13 plus or minus 2.5 days. In individual cases his tables (p. 327), however, show that the variation was from five to forty-four days.

Since the passage of food through the gastrointestinal tract requires considerably less time than from ten to fourteen days, the question arises as to whether the hemorrhage usually extends over a period of days. Meulengracht (*Brit. M. J.* 2:321 [Aug. 12] 1939) believes that "actual bleeding as a rule can last only a short time, perhaps only a few hours," and that the prolonged positive benzidine test is an indication of the time required for the intestine to rid itself of blood rather than an

indication of the duration of hemorrhage. In support of this view Meulengracht cites the work of Hesser (*Acta med. Scandinav.* supp. 59, p. 367, 1934) that patients with bleeding peptic ulcer gave evidence of having barium salts in their stools for from eight to twenty-one days following a barium sulfate meal.

Although a single hemorrhage of not more than a few hours duration may be the rule in peptic ulcer, it does not exclude the possibility that in some cases the bleeding may be more prolonged or may recur, as evidenced by the vomiting of bright red blood several days after the initial hematemesis or melena. However, the average figures are of value in an individual case in that when the stools become negative with the benzidine test it is known that the bleeding probably stopped from seven to fourteen days before.

Hemorrhage from lesions in the gastrointestinal tract other than that from peptic ulcers and esophageal varices is apt to be prolonged and with an indefinite termination. This applies particularly to hemorrhage arising in lesions of the colon. It is therefore extremely difficult to determine the duration of a positive benzidine test after the hemorrhage has ceased; however, it seems reasonable to think it would be somewhat less than that in hemorrhage from peptic ulcers.

BILATERAL PNEUMOTHORAX AND INTRA-ABDOMINAL SURGERY

To the Editor:—A woman aged 50 has bilateral pulmonary tuberculosis for which she is receiving bilateral pneumothorax therapy. At present her sputum is negative and the pulse rate and temperature are normal. She also has been having severe attacks of pain in the right hypochondrium presumably due to gallbladder disease. She has not responded to diet and medication. X-ray studies of the gallbladder have not been made. If further examination reveals the condition to be due to cholecystitis or cholelithiasis, would surgery be contraindicated because of the presence of bilateral pulmonary tuberculosis? If surgery is contraindicated, what alternative therapy would you suggest for the gallbladder condition?

Daniel Haffron, M.D., Elgin, Ill.

ANSWER:—Artificial pneumothorax, even bilateral artificial pneumothorax, is not an absolute contraindication to urgent abdominal surgery. Such surgery should be resorted to only when there is an urgent indication and when the diagnosis of abdominal disease is absolutely certain and specific. Patients with pneumothorax frequently have pleuritic pain which radiates into the upper part of the abdomen and which may even cause localized tenderness and spasm.

The patient in question might be operated on at the present time only if x-ray studies give certain evidence of the diseased gallbladder and the attacks are so frequent and severe as to threaten complications and as to be unendurable.

THREATENED ABORTION

To the Editor:—A woman aged 31 was not able to conceive for seven months. A basal metabolic test showed —17; the pulse was 60, blood pressure was 96 systolic, 60 diastolic, the Wassermann reaction negative. Thyroid substance from one-half to 3 grains (0.03 to 0.2 Gm.) was prescribed. At the time the next period was expected the patient complained of pains low in the abdomen, typical of the menstrual period. After six days of intermittent cramps and no showing of the period (the patient claimed a variation of only one to three days in the cycle) five daily injections of progesterone of 1 international unit each were given. The cramps subsided. For the first three months of pregnancy the patient had severe nausea and some vomiting. The thyroid dose of from 3 to 4 grains (0.2 to 0.26 Gm.) daily was continued. On entering the fourth month she noticed a bloody discharge of from 1 drachm (4 cc.) to 1 ounce (30 cc.). The patient was advised to take bed rest, and 5 international units of progesterone was used daily. She has been in bed for three weeks and the discharge has not diminished. In addition cramps are felt intermittently and at times they are so severe that codeine is necessary. Treatment still consists of 5 international units of progesterone daily, from 3 to 4 grains (0.2 to 0.26 Gm.) of thyroid, and vitamin E administered orally. Her basal metabolism is now —7. Is this therapy satisfactory? Have you any other suggestions? What are the chances of a successful full term pregnancy?

M.D., New York

ANSWER:—The patient has been bleeding continuously for at least three weeks in spite of treatment, so that the present status of the gestation should be determined. It is possible that the treatment has caused a delay in the natural evacuation by the uterus of an abnormal gestation. This is a rather common occurrence at the present time. It is entirely possible that the fetus has been dead for some time and is being retained in the uterus. Rarely a hydatidiform mole may produce a clinical picture such as that described. A hormonal test for pregnancy and a careful vaginal examination will determine whether the gestation is normal.

The management which has been followed in this case represents an example of acceptable therapy. Threatened or habitual abortion may be treated by a sufficient amount of thyroid to

bring the basal rate to normal, progesterone and possibly vitamin E in the form of wheat germ oil. Synthetic vitamin E, alpha-tocopherol, is available for experimental work but is not yet available for clinical use. One must remember that many abortions occur as a result of abnormal embryos or chorions. Of course, it is useless to prolong one of these abnormal pregnancies. Furthermore, the onset of bleeding and particularly its continuation over a period of a week or longer is often indicative of serious damage to the embryo or gestational sac. It is unwise to continue conservative treatment over too long a period for this reason. Recent statistics indicate that if a pregnancy which has threatened to abort continues to term there is no increased likelihood of malformed fetuses.

BUTOLAN FOR PINWORMS

To the Editor:—Since 1924 I have on occasion used butolan in the treatment of pinworm infestations. I used it as recommended in George Blumer's edition of Billings-Forchheimer's *Therapeutics of Internal Diseases*. The results have been uniformly successful and no bad effects have been noticed. (Quassia enemas were used in conjunction.) I now have a patient recovering from postpneumonia empyema who is infested. She is 9 years old. Is there any reason why butolan should not be used? I have never seen it mentioned in *The Journal*.

George Braunlich, M.D., Davenport, Iowa.

ANSWER:—No contraindications for the use of butolan have appeared in the limited literature on this drug; in fact, the users of butolan claim that it has been without any untoward effects.

The articles by Schickhardt (*München. med. Wchschr.* 67: 722 [June 18] 1920) and Francke (*Med. Klin.* 16: 758 [July 18] 1920) were the first to be published on the use of this drug for the treatment of oxyuriasis. They claimed good results but their criteria of cure were based on the alleviation of symptoms and on stool examinations rather than on an anal swab technic, which today is regarded as the most reliable procedure for the diagnosis of oxyuriasis. Other notes and articles apparently have been based on the results of these investigators.

At the present time the drug of choice for the treatment of oxyuriasis appears to be gentian violet given orally, as reported by W. H. Wright and F. J. Brady of the United States Public Health Service (*THE JOURNAL*, March 9, 1940, p. 861).

DIVISION OF SAPHEOUS VEIN IN VARICOSE ULCER OF LEG

To the Editor:—A white man aged 40 had varicose veins injected about ten years ago. A varicose ulcer appeared over the lower third of the same leg nine months ago following the gradual reappearance of the varicose veins. I suggested rest off his feet, which he refused, and he has been since under other doctors' care with various ointments without results. I am wondering whether there is a contraindication for the ligation of the internal saphenous vein because of the presence of the ulcer and also what suggestions can be offered for the handling of this problem.

M.D., Connecticut.

ANSWER:—The high division of the long saphenous vein and its tributaries at the groin is indicated in the presence of a leg ulcer when (1) there is no acute inflammation at the site of the ulcer, (2) acute lymphadenitis is not present in the groin, (3) there is evidence of marked reflux of blood through incompetent valves of the long saphenous vein and (4) there is no evidence of deep venous obstruction. The last contraindication seldom exists, for even if there is a good history of deep thrombophlebitis the thrombus frequently canalizes or is compensated by deep venous collaterals. The ulcer may not heal even after the high division of the saphenous vein and obliteration of the distal segment by injections if there is a severe thrombophlebitic induration surrounding the ulcer. If such is the case, weekly applications of glycerin-gelatin casts may be helpful in softening the induration and healing the ulcer. For resistant ulcers it may be necessary to resort to a major surgical procedure consisting of a wide excision of the fibrosed connective tissue, including the fascia.

SENSITIZATION TO DIGITALIS

To the Editor:—In reference to sensitization to digitalis (*Queries and Minor Notes*, *The Journal*, Sept. 28, 1940, p. 1122) there is little or nothing mentioned about systemic reactions but there are some reports of cutaneous response. A dermatitis may result from the external application of the fresh leaves of foxglove. The ingestion of this drug may cause macular and papular eruptions (Hydel, an erysipeloid eruption (Traube, Schuchardt) and a generalized erythroderma (Morrow, P. A.: *Drug Eruptions*; Selected Monographs in Dermatology, New Sydenham Society edited by T. Colcott Fox, London, 1893). There are a few other old references on cutaneous eruptions from the ingestion of digitalis. The following two are more recent: Pulch, A.: *Montpellier méd.* 73: 235 (April 15) 1930. Brandt: *Dermat. Wchschr.* 103: 726 (June 12) 1937.

E. William Abramowitz, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examination of boards of medical examiners and boards of examiners in the basic sciences were published in *THE JOURNAL*, November 23, page 1824.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, February. Part III. Boston during November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written*. Various centers, Feb. 20. Final date for filing application is December 21. *Oral*. Part II. Cleveland, May 31-June 1. Final date for filing application is April 1. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral*. Chicago, Dec. 6-7. Applications for Group A are closed. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Parts I-A and I-B, Feb. 17. Final date for filing application is Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Part II, Groups A and B, Cleveland, May 28-June 1. Final date for filing application is March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral*. Cleveland, May or June. *Written*. Various centers, March 8. The only written examination during 1941. Applications must be on file not later than Dec. 1. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written*. Cleveland, June 1-2. Final date for filing application is May 1. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, March 30-31, following the Region I meeting of the American Academy of Pediatrics. Chicago, May 18, following the Region III meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY. *Oral*. Cleveland, May 30-June 1. Final date for filing application is April 15. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

Alabama Reciprocity Report

Dr. J. N. Baker, secretary, Alabama State Board of Medical Examiners, reports twenty-one physicians licensed to practice medicine by reciprocity from April 25 through September 25. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Emory University School of Medicine.....	(1937), (1939)		Georgia
Tulane University of Louisiana School of Medicine (1929), (1938, 2), (1939) Louisiana			
Johns Hopkins University School of Medicine.....	(1931)		Maryland
Harvard Medical School.....	(1928)		Ohio
University of .. School ..	(1936)		Michigan
Washington Medicine.....	(1938, 2)	Missouri
University of Medicine.....	(1934)	Ohio
University of Medicine.....	(1938)	Oklahoma
Hahnemann of Philadelphia (1937)		Penna.
Medical College of the State of South Carolina.....	(1939)		S. Carolina
University of Tennessee College of Medicine.....	(1931), (1937, 2)		Tennessee
Vanderbilt University School of Medicine.....	(1938), (1939)		Tennessee
Queen's University Faculty of Medicine.....	(1938)		New York

Pennsylvania July Report

Miss Marguerite G. Steiner, acting secretary, Bureau of Professional Licensing, reports the written examination for medical licensure held at Philadelphia and Pittsburgh, July 9-13, 1940. The examination covered five subjects and included fifty questions. An average of 75 per cent was required to pass. Four hundred and seventy-two candidates were examined, 450 of whom passed and twenty-two failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
College of Medical Evangelists.....	(1935), (1939), (1940)		3
Yale University School of Medicine.....	(1939)		1
George Washington University School of Medicine.....	(1939, 2)		2
Georgetown University School of Medicine.....	(1938), (1939, 10)		11
Howard University College of Medicine.....	(1939, 4)		4
Loyola University School of Medicine.....	(1940, 2)		2
Northwestern University Medical School.....	(1939), (1939)		4
Rush Medical College.....	(1937)		1
Indiana University School of (1939, 2)		2
University of Louisville School (1939)		1
Tulane University of Louisi (1939, 3)		5
Johns Hopkins Univ. School (1939, 4), (1939, 3)		7
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1935), (1938, 2), (1939, 2)	5
Harvard Medical School (1935), (1938, 2), (1939, 2)		2
Tufts College Medical School.....	(1938), (1939)		1
University of Michigan Medical School.....	(1939)		1
St. Louis University School of Medicine.....	(1939, 3)		3

University of Nebraska College of Medicine.....	(1939)	1
Cornell University Medical College (1930), (1938), (1939, 2)		4
University of Buffalo School of Medicine.....	(1939, 2)	2
Univ. of Rochester School of Medicine and Dentistry (1939)		1
Duke University School of Medicine.....	(1939)	1
Eclectic Medical College, Cincinnati.....	(1939, 5)	5
Western Reserve University School of Medicine.....	(1939, 2)	2
University of Oklahoma School of Medicine.....	(1938)	1
Hahnemann Medical College and Hospital of Philadelphia	(1938, 2), (1939, 66)	68
Jefferson Medical College of Philadelphia (1937, 3), (1938, 20), (1939, 49), (1939, 2)* 74		
Temple University School of Medicine (1936), (1938, 17), (1939, 61) 79		
Univ. of Pennsylvania School of Med. (1937, 3), (1938, 26), (1939, 42) 71		
Univ. of Pittsburgh School of Medicine.....	(1938), (1939, 49)	50
Woman's Medical College of Pennsylvania.....	(1938), (1939, 11)	12
Medical College of the State of S. Carolina (1936) (1939, 3)		4
University of Tennessee College o ..		2
University of Texas Faculty of ..		1
University of Texas School of ..		1
University of Virginia Department ..		1
Marquette University School of Medicine.....	(1937)	1
Dalhousie University Facul ..		1
University of Toronto Faci ..		1
McGill University Faculty ..		2
Medizinische Fakultät der ..		2
Hamburgische Universität ..		1
Regia Università degli Studi di Perugia. Facoltà di ..		
Medicina e Chirurgia	(1937)	1
Regia Università di Napoli Facoltà di Medicina e ..		
Chirurgia	(1938, 2)	2
Licentiate of the Royal College of Physicians, of the ..		
Royal College of Surgeons of Edinburgh and of the ..		
Royal Faculty of Physicians and Surgeons of Glasgow (1937)		1
University of Glasgow Medical Faculty.....	(1929)	1
Universität Basel Medizinische Fakultät.....	(1937), (1938)	2

School	FAILED	Year Grad.	Number Failed
St. Louis University School of Medicine.....	(1939)		1
Hahnemann Med. College and Hosp. of Philadelphia (1939, 10)			10
Temple University School of Medicine.....	(1939, 2)		2
University of Pittsburgh School of Medicine.....	(1939, 2)		2
University of Virginia Department of Medicine.....	(1938)		1
Medizinische Fakultät der Universität Wien.....	(1933)		1
Christian-Albrechts-Universität Medizinische Fakultät, ..			
Kiel	(1913)		1
Ludwig-Maximilians-Universität Medizinische Fakultät, ..			
München	(1938)		1
Magyar Királyi Pázmány Petrus Tudományegyetem ..			
Orvosi Fakultása, Budapest	(1915)		1
Regia Università di Napoli Facoltà di Medicina e ..			
Chirurgia	(1938)		1
Université de Lausanne Faculté de Médecine.....	(1930)		1

* License has not been issued.

South Carolina June Report

Dr. A. Earle Boozer, secretary, State Board of Medical Examiners of South Carolina, reports the oral and written examination for medical licensure held at Columbia, June 24-26, 1940. The examination covered seventeen subjects and included fifty-two questions. An average of 75 per cent was required to pass. Forty candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Loyola University School of Medicine.....	(1940)		81.9
Tulane University of Louisiana School of Medicine.....	(1940)		84.2
Johns Hopkins University School of Medicine.....	(1932)		81
University of Nebraska College of Medicine.....	(1939)		83.6
Columbia University College of Physicians and Surgeons (1919)			89
Jefferson Medical College of Philadelphia.....	(1940)		79.7
University of Pennsylvania School of Medicine.....	(1929)		79.9
(1939) 82.1			
Medical College of the State of South Carolina.....	(1940)		79
81.1, 81.5, 81.5, 82.7, 83, 83.2, 83.9, 84, 84, 84.1,			
84.4, 84.5, 84.6, 84.6, 85.2, 85.4, 85.5, 85.6, 85.6,			
85.7, 85.7, 85.9, 85.9, 86.2, 86.7, 86.7, 88.1, 89, 89.6,			
89.7, 92			

Fifteen physicians were licensed to practice medicine by reciprocity and one physician so licensed by endorsement on May 1, June 25 and July 11. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Emory University School of Medicine.....	(1923), (1937)		Georgia
University of Georgia School of Medicine.....	(1936)		Georgia
Rush Medical College.....	(1937)		Alabama
University of Cincinnati College of Medicine.....	(1933)		Ohio
Western Reserve University School of Medicine.....	(1938)		Ohio
University of Oklahoma School of Medicine.....	(1937)		Oklahoma
Jefferson Medical College of Philadelphia.....	(1932), (1938)		N. Carolina
(1937) Pennsylvania			
University of Tennessee College of Medicine.....	(1937)		Tennessee
Baylor University College of Medicine.....	(1919)		N. Carolina
Medical College of Virginia.....	(1930, 2)		N. Carolina
University of Virginia Department of Medicine.....	(1931)		Virginia

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Duke University School of Medicine.....	(1936)		N. B. M. Ex.

Book Notices

Modern Dermatology and Syphilology. By S. William Becker, M.D., Associate Professor of Dermatology and Syphilology, Kuppenheimer Foundation, University of Chicago, and Maximilian E. Obermayer, M.D., Assistant Professor of Dermatology and Syphilology, Kuppenheimer Foundation, University of Chicago. Cloth. Price, \$12. Pp. 371, with 493 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1940.

Here is a distinctly new volume in the field of textbooks on dermatology. The book has been planned primarily as a textbook and contains several new features both as to arrangement and as to nature of material which will make it appeal to the medical student. The functional point of view has been dominant. Skin diseases are grouped according to common causation or diagnostic considerations which make natural grouping. There is a general consideration of therapy as has been the custom with other textbooks on diseases of the skin, but in addition special information is provided in relationship to each group of diseases. The bibliography for each chapter is brief but useful. There are thirty-two colored illustrations and a great number of illustrations in black and white, which naturally are of special value in a work on diseases of the skin. Another new feature is a chart of the treatment of syphilis worked out according to the technic of the University of Chicago Clinics but guided largely by the decisions of the Cooperative Group. A chart of this type is obviously useful as a guide to the general practitioner. The book is printed in two narrow columns, which make reading easy. The style is direct and the volume has been well edited. This book will constitute not only a textbook for students but also an exceedingly good reference book in its field. The section on syphilis concludes the volume and the section itself is concluded with a discussion of the social aspects of the disease and the public effort against it. This is, of course, unique for a textbook on diseases of the skin and syphilis. Progress in this field has been so rapid that this chapter is well nigh obsolete with its date of publication. A good index completes what is an exceptional volume.

Endocrine Therapy in General Practice. By Elmer L. Serrinhaus, M.D., F.A.C.P., Professor of Medicine, University of Wisconsin, Madison. Third edition. Cloth. Price, \$2.75. Pp. 238, with 49 illustrations. Chicago: Year Book Publishers, Inc., 1940.

This edition includes a number of revisions throughout the various chapters and also a new chapter on the endocrine problems in childhood and adolescence. The book is intended to be an elementary textbook on endocrine therapy. It includes brief discussions of diagnosis and etiology of the various disturbances. The larger portion is devoted to the use of various agents in the treatment of endocrine disorders. The book is valuable in that it explains in a simple manner the many common endocrine disturbances and their treatment. It does not confuse the untrained reader with discussions on atypical and rare disorders but limits itself to cases which the general practitioner is most apt to meet. In this way a clear understanding of endocrine therapy is available for the general practitioner. The book is valuable in that it demonstrates that there is no need to consider endocrine therapy a mysterious, complicated and difficult task if the fundamental principles of physiology are adhered to. On the other hand, the author seems to evince undue optimism toward therapeutic procedures which are still in an experimental stage. The stimulation treatment of the ovaries with the various gonadotropins is still most uncertain, even in the hands of the specialist, and it appears inadvisable to recommend specific treatment to the untrained practitioner with these substances. Certainly the results with pregnant mare serum gonadotropin do not justify its use by the general practitioner. This is reflected in the statement on page 188 that preparations of pregnant mare serum gonadotropin "are probably effective stimulators of testicular tissue growth and function." In addition, the treatment of pituitary dwarfism does not appear to be as promising as the author maintains. In fact, it is surprising that the author considers it possible to overtreat with growth hormone and produce an acromegalic condition (p. 195) when, as a matter of fact, the growth hormone preparations available commercially are notoriously weak. Unfortunately the author

refers repeatedly to proprietary endocrine preparations and the firms which market these products. This procedure aids in the promotion of certain products which may not have been examined and approved by official organizations on pharmaceuticals and, on the other hand, discriminates against other preparations which might be equally effective.

Pathology. By Eugene C. Piette, M.D., Pathologist and Director of the Clinical Laboratories of the West Suburban Hospital, Oak Park, Illinois. Third edition. Cloth. Price, \$2. Pp. 247, with 60 illustrations. Philadelphia: F. A. Davis Company, 1940.

Although the title of this book gives no indication of its purpose, the introduction and text suggest that it is intended for nurses. In addition to a short review of the meaning of terms used in pathology there are also appended directions for collecting, labeling and examining specimens destined for a laboratory of clinical pathology. The appropriateness of writing a pathology for nurses might well be questioned. Possibly they should have their minds and their time fully occupied with their own specialty, without any dabbling in the jargon of the medical sciences. But if modern standards force them to learn the special language of pathologists, then, at least, instruction in this line should be accurate and down to date. This book falls short in both of these requirements. Beginning as a sort of amplified dictionary, it becomes a potpourri of pathologic descriptions, symptoms, treatment and admonitory advice. For example:

Page 20. "If there is a pathologist in the hospital, the nurse must call him immediately after the thyroid is removed."

Page 24. "Vitamin A—antiophthalmic and anti-infective . . ."

Page 39. "Arteriosclerosis is a disease of advanced age . . . In still another case the arteries of the pyloric part of the stomach or duodenum become thickened, hyalinized, and their lumen becomes obliterated while the patient is still in his thirties and shows no other signs of sclerosis. This may cause a peptic ulcer."

Page 42. "Only the stones (in gallbladder) which contain a certain amount of calcium cast a shadow on x-ray examination."

Page 54. "Peptic ulcer (gastric and duodenal), according to a modern conception, is also an infarct."

Page 56. "Frequently this death (from embolism) occurs after slight exertion, sitting up or turning over, against the doctor's orders."

Page 61. "In the temperate zone syphilis is the most important causative agent in local enlargements of an organ such as the leg, scrotum, etc."

Page 93. "This mouth breathing may lead to heart lesions, arthritis, and nephritis."

Page 99. ". . . Infected hemorrhoids, may lead to inflammation of the portal vein (pyelphlebitis) . . ." "Peptic ulcer . . . is probably always an infarct."

Page 109. ". . . diseases of the skull bones (otitis) . . ."

Page 161. "The tumors composed of nerve tissue are rare."

Page 187. "Some patients prefer not to disclose their identity and the pseudonym of John Doe is most popular in these instances. It is probably advisable not to express any signs of having heard this name before."

Two further objections are to be added. One is the character of the illustrations. One of them, for instance, was taken from Billroth and most of the others might accompany a book written a hundred years ago but certainly are not worthy of modern publications. The other objection is the fact that an attempt has been made to instruct the nurses in regard to clinical pathologic procedures. Not only is the instruction inadequate, but in some instances it is not correct.

Problems of Nervous Anatomy. By J. Boeke, LL.D., Professor of Histology and Embryology, the University of Utrecht, Utrecht. Cloth. Price, \$2.75. Pp. 161, with 48 illustrations. New York & London: Oxford University Press, 1940.

This little book contains the substance of three lectures delivered at the Universities of London and Oxford in 1937 and of a lecture delivered before the Anatomische Gesellschaft the same year. The book is divided into four chapters corresponding to these four lectures and dealing with (1) changes in the spinal and sympathetic innervation of the skin during degeneration and regeneration, (2) the sympathetic ground plexus in the glands, muscles and connective tissues of the body, (3) the problem of the "interstitial cells" in the sympathetic nervous system: their relation to neurons, and the innervation impulse as a humoral change in the tissues, and (4) the present state of the neuron doctrine and our knowledge of the synaptic junctions between the nerve cells themselves and between nerve cells and end organs. The second and third chapters contain a clear statement of the author's conception of the connections between the sympathetic nerve fibers and the innervated tissues, i. e. the glands, smooth muscles and, strangely enough, also connective

tissue. This connection consists of a continuous unbroken net of very "delicate interwoven and anastomosing nonmyelinated nerve fibers, running in strands or flattened bands of extremely delicate neurofibrillae with scattered nuclei, forming the terminations of the sympathetic plexuses" and including many "interstitial" cells. These interstitial cells, which many authors have regarded as connective tissue elements, are interpreted as nerve cells. Since the individual nerve fibers of the sympathetic nerves are thought to lose themselves in this diffuse network, the individual sympathetic neurons are diffusely connected at the periphery. Boeke accepts without question the conception of a humoral transmission of nerve impulses and he believes that the diffuse terminal net which he describes is especially adapted to this mode of transmission. The concluding chapter contains a not very illuminating argument against the validity of the neuron theory. The illustrations are excellent and present very well the conception of the terminal net. They are all interpretative drawings and as such lack the objectivity of photomicrographs. The book is a valuable contribution to a controversial subject but is to be taken as an expression of the author's personal convictions rather than as presenting a final solution of the problems discussed.

Textbook of Biochemistry. By Benjamin Harrow, Ph.D., Professor of Chemistry, City College, College of the City of New York. Second edition. Cloth. Price, \$3.75. Pp. 439, with 88 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

One would expect that the new edition of Harrow's textbook should prove to be popular for a first course in biochemistry and for medical or dental students. Indeed, most medical practitioners will find it a valuable book for a succinct review of biochemistry. It is clearly and simply written, presupposes little knowledge of biochemistry on the part of the reader, and adequately presents the main outlines of the subject. The author first considers the chemistry of carbohydrates, fats, proteins, nucleoproteins and enzymes. He then discusses the subjects of foods and vitamins and of syntheses in the plant kingdom. This leads logically to a consideration of digestion and absorption by the animal body and the mechanism of metabolism and excretion of foodstuffs. Obviously, in a book intended to serve as a textbook it is impossible to cover in great detail the tremendous advances which have been made in biochemistry in the last two decades. Nevertheless Dr. Harrow has succeeded in incorporating wherever possible the most modern developments and interpretations. This is clearly illustrated in the chapters on vitamins and hormones. An excellent practice has been followed in the choice of references for the various chapters. Individual papers have been selected with a view to training the student in the experimental method of approach. The emphasis in the bibliography has been placed on critical, modern reviews. The book contains numerous well chosen illustrations and a five page appendix on the nutritive value of foods.

La correction des téguments et des formes. Par le Professeur Pierre Sebillan. Paper. Price, 33 francs. Paris: Masson & Co, 1939.

This work encompasses a thorough but unpadding review of the entire field of plastic surgery. All phases of reconstruction are discussed in an engaging manner. The author is well known in France as an authority on the subject. Deformities of the face, including the nose, lips, jaws and ear, are thoroughly discussed and effectively illustrated by photographs and line drawings. There are also chapters on harelip, cleft palate, and so on. The author gained a great deal of experience in this type of work under Morestin, Sebillan and others during and after the war of 1914-1918. The world conflict demanded competence in reparative surgery for facial injuries, and it seems that recent events hold up in bold relief the necessity of possessing knowledge for effective reconstruction work on the face. The book opens with a discussion of generalities. The author stresses prompt emergency esthetic surgery, pointing out that many bad results follow neglect of proper primary care of wounds. The operative procedures described are pretty well standardized; the author describes those which in his hands have proved most effective. He uses by preference cartilage instead of bone transplants in operations about the nose. The bibliography following each chapter is a valuable addition to the work, ena-

bling the reader interested in any particular phase of the subject to familiarize himself with contemporary writings on the subject. All in all, the work is a well rounded out volume and can be recommended to all who are interested in the subject and who are conversant with the French language.

Elmer and Rose Physical Diagnosis. Revised by Harry Walker, M.D., F.A.C.P., Associate Professor of Medicine, Medical College of Virginia, Richmond, Va. Eighth edition. Cloth. Price, \$8.75. Pp. 792, with 293 illustrations. St. Louis: C. V. Mosby Company, 1940.

This volume is a new edition of the popular book on physical diagnosis by Elmer and Rose reedited by Dr. Harry Walker. The author states in the introduction to this edition that the book is to be a guide to students of medicine and to general medical practitioners. The author is one who has had considerable experience in teaching and in the practice of medicine, and he therefore can speak from knowledge gained by his own personal efforts. The book covers the entire problem of the bedside approach to clinical medicine from the standpoint of physical diagnosis and, in addition, there is incorporated in it quite a comprehensive bit of information concerning special procedure. The impression is that the author has used keen discrimination in his effort to evaluate the importance of both physical methods and the so-called procedures of precision. The first section of the book is taken up with the art of physical diagnosis and the physical changes which result in a modification of normal physical phenomena. The second section deals with special diseases and their important physical signs. The section which deals with physical diagnosis in neuropsychiatric patients is a distinct disappointment. This was not written by the author, and hence he is not responsible for the careless construction and numerous loose statements. This chapter should certainly be rewritten in the next edition and a large mass of uncertain and doubtful data eliminated. As a whole, the book is a commendable one and should have the justifiable support of those who find a book of this type obligatory in clinical medicine.

Diseases of the Nervous System. By W. Russell Brain, M.A., D.M., F.R.C.P., Physician with Charge of Out-Patients to the London Hospital, London. Second edition. Cloth. Price, \$9.25; 30s. Pp. 950, with 77 illustrations. New York & London: Oxford University Press, 1940.

A second edition of this useful compendium is welcome. Its compact lucid accounts of neurologic disorders are attractive and useful to students. The latest advances in neurologic knowledge have been included as far as they seem well established. In addition a useful new chapter has been added on the psychologic manifestations of organic nervous disease. In order to make room for this chapter without enlarging the book, the author has wisely omitted a discussion of endocrine disorders. Some new illustrations appear but, as in the first edition, seem to have been inserted haphazardly and add little to the book. The discussion of the neuroses might well have been omitted; not only is it too brief to be of any value but this subject is now adequately discussed in every psychiatric textbook. But only twenty-four pages of this book are occupied by the neuroses, so that this is not a serious defect. The discussions of neurophysiology and neuropathology are inadequate but, since these subjects are well presented in most American medical schools, this manual is quite satisfactory as a clinical guide.

Physiology and Anatomy. By Esther M. Grelshelmer, B.S. in Education, M.A., M.D., Professor of Physiology, Woman's Medical College of Pennsylvania, Philadelphia. Fourth edition. Cloth. Price, \$3.50. Pp. 822, with 474 illustrations. Philadelphia, Montreal & London: J. P. Lippincott Company, 1940.

This edition is thoroughly revised and reset to meet the most recent trends in teaching the subject. The subject matter has been arranged on the unit plan and consists of five units: the body as an integrated whole, the erect and moving body, integration and control of the body by the nervous system, maintaining the metabolism of the body and the reproductive system. The teacher's manual for use with the text is written by Miss Ostlie and prefaces each unit. The manual consists of thirty-six lectures and laboratory demonstrations which are most practical for the instruction of the student. In spite of the fact that the book is devoted to two subjects there is a definite text separation of them and the book can be used for separate courses in anatomy and physiology. The organization is excellent. The

written material is enhanced by helpful illustrations and each chapter is practically crystallized by summaries; some chapters contain a concise discussion of the application of the didactic material to clinical conditions. The material is presented in a terse and logical manner. It is explicit and graphic and is carefully edited. The illustrations are carefully selected and well done. The book is current and authoritative and is written in a lucid and engaging style. It should find popular acceptance among teachers of physical education and nurses. Its use is, however, not limited to these groups. Because of its simplicity in presentation it could profitably serve other groups of students who are interested in the study of human anatomy and physiology.

A Textbook of Physiology. By William H. Howell, Ph.D., M.D., ScD. Fourteenth edition. Cloth. Price, \$7.50. Pp. 1,117, with 330 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

The author again has brought his book down to date. His guiding principles have been the importance of simplicity and clearness in presenting facts and theories, and the need of limitation of material that must be selected from a bewildering number of researches that have been published in physiology and the related sciences. Amid the conflicting results of this mass of literature, the best that an author can do is to give as clear a picture as possible of the tendencies of the time. There are numerous illustrations, a few of which are beautifully reproduced in color; and yet it seems that the book would be more valuable to students had there been a still larger number of carefully selected illustrations.

Atlas der Hals-, Nasen-, Ohrenkrankheiten: Eine Sammlung typischer Krankheitsbilder mit topographischen, diagnostischen und therapeutischen Hinweisen. Von Dr. Carl von Elcken, ord. Professor an der Universität Berlin, und Dr. A. Schulz van Treeck, Assistent der Universitäts-Hals-, Nasen-, Ohrenklinik der Charité, Berlin. Cloth. Price, 32 marks. Pp. 199, with 461 illustrations. Leipzig: Georg Thieme, 1940.

This fine work cannot be too highly praised. It is a magnificent tribute to the otolaryngologic, not to mention the publisher's, art. The portion devoted to text is minimal. For the larger part this atlas depicts familiar conditions in the ear, nose and throat. Less commonly seen situations are by no means neglected, however. The larger number of reproductions of disease conditions are in color so masterfully executed that the pleasure derived in gazing at them almost equals the informative aspect. In the section devoted to otology alone the illustrations number over 125, and similarly those relating to the nose, larynx and pharynx are generously apportioned. Intended chiefly for students and general practitioners, this work is nevertheless of great value to the specialist. Besides the disease conditions so beautifully portrayed there are adequate sections relating to topographic anatomy and therapeutic interventions.

The Public Health Nurse and Her Patient. By Ruth Gilbert, Supervisor of Social Work, Psychiatric Service in the Community, New Haven. Cloth. Price, \$2.25. Pp. 396. New York: Commonwealth Fund; London: Oxford University Press, 1940.

This book is of interest primarily to nurses engaged in public health nursing. It is a study of the nurse's mental attitude and the philosophy of her work as it involves her relationship with patients, other nurses and co-workers. Originally entitled "Mental Hygiene in Public Health Nursing," it deals with situations which confront the nurse in her work. It contains chapters on nurses' attitudes, patients' attitudes, physical defects and injuries, mental defects and disease, the building of relationships, the nurse and her group, the nurse and the maternity patient, the child in his family and nursing problems related thereto, and familiar training situations relating to the training of the infant. A chapter is devoted to interagency relationships. Except for casual references there is no adequate discussion of the relationship of the public health nurse to the practicing physician, although this constitutes one of the most important and frequently disastrous relationships, especially with inadequately trained nurses working under insufficient supervision. The term "physician" and its equivalent "doctor" do not appear in the index, nor are medical relationships indexed under that heading.

Except for this inadequacy, the book should be extremely useful to the public health nurse and not without value to the

private duty nurse, since patients are patients regardless of the label which may be affixed to the nurse who is serving them. Unlike much professionally self-conscious literature, this book is not a bore but is distinctly readable. Like all publications of the Commonwealth Fund, it is beautifully printed and bound.

A Manual of Otolaryngology, Rhinology and Laryngology. By Howard Charles Ballenger, M.D., F.A.C.S., Assistant Professor of Otolaryngology, Northwestern University School of Medicine, Chicago. Cloth. Price, \$3.75. Pp. 302, with 94 illustrations. Philadelphia: Lea & Febiger, 1940.

The author has endeavored to produce a textbook chiefly for the use of undergraduate students. Such a work needs to be made concise, and in the effort to be brief arise all the possibilities for errors in judgment as to what to and what not to retain. The ideal textbook for students would abound in numerous illustrations of anatomic, histologic and pathologic importance. Their number would of necessity reduce their size and so for clarity's sake they ought to be in large part semidiagrammatic. Most of the illustrations have a familiar appearance. They appear to come from the author's larger and much older work, and it is a pity that an entirely new set was not prepared. In most other respects the author has done well. His clinical judgment is distinguished by good sense, he is not an enthusiast for indiscriminate surgical intervention and he is familiar with important recent advances in the physiology of his field.

Standardized Tests and Educational Practice. By Ellsha F. Bliss Jr. Paper. Price, 75 cents. Pp. 29. Brooklyn, N. Y.: The Author, 1940.

This pamphlet seems to express a deep-seated and intense, but rather vague, resentment and dissatisfaction with the existing methods by which intelligence, aptitude and other psychologic tests are employed in the schools. An ordinance is proposed by means of which the purchase, preparation, administration and interpretation of such tests could supposedly be regulated, although the pamphlet also condemns what it calls political regulation while recommending an ordinance to be adopted by local political bodies, plus federal regulation. The text of the ordinance and the involved cumbersome style in which the pamphlet is written make it extremely difficult to interpret. There is, in fact, no assurance that the central idea, if any, contained in this pamphlet is not so deeply buried in words that it is not totally incomprehensible.

Insurance of the Expense of Medical Service. By Wendell A. Millman. [Reprinted from the Transactions of the Actuarial Society of America, Vol. XLII, Part I, No. 103, May 1940]. Paper. Pp. 114-149. New York, 1940.

This pamphlet is almost the only attempt to apply actuarial calculations to the problem of insurance of the expense of medical service. The peculiar effect on actuarial calculations of the relations between medical service needed and medical service sought under the influence of insurance is noted, as is also the analogous difficulty of exercising professional control over the amount and quality of service given. Practically all the worthwhile studies of costs of medical care and income of physicians are utilized and several insurance schemes are discussed. Elements in medical service which are insurable are analyzed and some of the methods of control of the more hazardous elements are discussed.

Le syndrome de désintégration phonétique dans l'aphasie. Par Th. Alajouanine, professeur agrégé à la Faculté de médecine de Paris, André Ombredane, directeur-adjoint du laboratoire de psycho-biologie de l'enfant à l'Ecole pratique des hautes-études, et Marguerite Durand, assistante à l'Institut de phonétique. Paper. Price, 80 cents. Pp. 138, with 44 illustrations. Paris: Masson & Cie, 1939.

The authors have made a careful study of the disturbances of speech in the aphasic. For their phonetic studies they have used graphic registration of the sound waves and describe in detail the variations from normal. This is an interesting study of the peripheral manifestations of a central speech disorder.

Allergy. By Leo H. Crip, M.D., Consultant, Veterans' Administration, Pittsburgh. In collaboration with the Division of Post Graduate Instruction and Medical Research, Medical and Hospital Service, Veterans' Administration. Veterans' Administration Medical and Hospital Service, Clinical Bulletin No. 29. Paper. Price, 10 cents. Pp. 60. Washington, D. C.: Supl. of Doc., Government Printing Office, 1940.

This is a brief discussion of the present status of knowledge of anaphylaxis and allergy in man. As an introduction to the subject it should be useful. Its scope is rather limited.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Compensability of Death from Lobar Pneumonia.—The workmen's compensation act of North Dakota provides: "The term 'injury' includes in addition to any injury by accident, any disease proximately caused by the employment." Tweten, an employee of Wells County, N. D., contracted lobar pneumonia following a soaking received while performing outside work on the fair grounds during cold and rainy weather. He died as the result of the pneumonia. His wife, the claimant, filed a claim for compensation under the workmen's compensation act of North Dakota. Her claim was rejected by the North Dakota workmen's compensation bureau. This ruling was reversed by the district court, Wells County, N. D., and judgment was rendered for the claimant. On appeal to the Supreme Court of North Dakota the judgment for the claimant was affirmed and the workmen's compensation bureau petitioned that court for a rehearing.

The medical testimony, said the Supreme Court, was in accord that exposure to cold and inclement weather frequently is a contributing cause of pneumonia. In the judgment of the court there was no question but that the deceased died from lobar pneumonia contracted as a result of exposure to inclement weather in the course of his employment. The court could not agree with the workmen's compensation bureau's contention that the disease from which Tweten died was not a compensable "injury" within the meaning of the workmen's compensation act of North Dakota. The court pointed out that a Texas case, *Amann v. Republic Underwriters*, 100 S. W. (2d) 778, on which the bureau relied and which denied compensation under circumstances similar to those in the instant case, was decided under the Texas workmen's compensation act, which differs from the North Dakota act and defines a compensable injury to be "damage or harm to the physical structure of the body and such diseases or infection as naturally result therefrom." The language in the Texas act makes compensable only such diseases as are caused by a prior physical injury rather than by a particular employment. Under the North Dakota act, however, even prior to the enactment of the 1925 amendment quoted above, a physical impact was not a necessary prerequisite to a compensable "injury." In the opinion of the court the 1925 amendment merely enlarged the meaning of the term "injury" and included within its meaning any disease proximately caused by the employment. The court concluded, therefore, that to be compensable a disease need not arise from, or be directly traceable to, some physical impact or hurt, and so it held that Tweten's death from pneumonia was compensable. Accordingly, the petition for a rehearing was denied and the judgment for the claimant was upheld.—*Tweten v. North Dakota Workmen's Compensation Bureau (N. D.)*, 287 N. W. 304.

Medical Practice Acts: Right of Physician and Corporate Employer to Enjoin Board of Examiners from Revoking Physician's License.—Fisch, a physician licensed to practice in Minnesota, agreed with an incorporated social and fraternal organization to render medical services to members of the organization and to their families. Apparently, Fisch was paid directly by the organization, but whether on a monthly salary or on a fee basis the reported decision does not state. Without the payment of additional charges other than their membership fees in the organization, members of the organization and their families were entitled to medical services from Fisch. Fisch and the fraternal organization sought to enjoin the board of medical examiners of Minnesota from instituting proceedings to revoke Fisch's license to practice in Minnesota, based on the theory that Fisch was guilty of unprofessional conduct because of his connection with the corporation. The plaintiffs alleged that the threatened action of the board would

be an interference with the contractual relationship existing between them. The trial court dismissed the action and the plaintiffs appealed to the Supreme Court of Minnesota.

It is apparent, said the Supreme Court, that what the plaintiffs really seek by this action is a judicial determination that the contract between them is a valid one; in other words, what they actually seek is the equivalent of a declaratory judgment. Since the board of medical examiners is a body organized and existing by virtue of legislative enactment, courts must exercise extreme caution in passing on its actions, especially if what the board proposes to do and what the plaintiffs want enjoined lies within the jurisdictional authority of the board. Unquestionably, the Minnesota medical practice act authorizes the board to "suspend or revoke the license of, any person guilty of immoral, dishonorable, or unprofessional conduct, but subject to the right of the applicant or licentiate to appeal to the district court in the proper county on the questions of law and fact." (3 Mason Minn. St. 1940 Supp., Sec. 5707.) As to what constitutes "immoral, dishonorable, or unprofessional conduct" the statute affords adequate definitions. As to Fisch, the sole question is whether or not he has an adequate remedy at law under the section just referred to. If he has, then courts have no right to interfere except as provided by the law presented, i. e., to review on appeal "the questions of law and fact." The board has jurisdiction to proceed against any member of the medical profession, and adequate means are afforded on hearings held by the board for the accused physician to make any showing material to the issues made on any charge brought against him. Review from the board's decision is provided, hence the legal remedy is there and obviously is ample. As to the physician, therefore, in the judgment of the court the trial court clearly was right in dismissing the suit.

As to the corporate plaintiff, the fraternal organization, continued the court, it is apparent that its sole desire is to enjoin the board from proceeding against its physician employee. It has no license or right of its own of or concerning which the board has any jurisdiction. It cannot "interfere" with any proceedings that may be brought by the board against the physician employee. By joining their forces the plaintiffs cannot add one whit to their alleged cause. If that could be done, the board in practically every case would be handicapped and perhaps prevented from proceeding against any practitioner, since even a quack would be likely to get some one to join him in an injunction suit.

The Supreme Court accordingly confirmed the order of the trial court dismissing the suit.—*Fisch v. Sivertsen et al., Comprising State Board of Medical Examiners (Minn.)*, 292 N. W. 758.

Society Proceedings

COMING MEETINGS

- American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 19-21. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.
- American Society of Anesthetists, New York, Dec. 12. Dr. Paul M. Wood, 745 Fifth Ave., New York, Secretary.
- American Student Health Association, Ann Arbor, Mich., Dec. 27-28. Dr. Ralph I. Canuteson, University of Kansas, Lawrence, Kan., Secretary.
- Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otolological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.
- Puerto Rico, Medical Association of, San Juan, Dec. 13-15. Dr. David E. Garcia, P. O. Box 3866, Santurce, Secretary.
- Radiological Society of North America, Cleveland, Dec. 2-6. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
- Society of American Bacteriologists, St. Louis, Dec. 27-29. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
- Southern Section, American Laryngological, Rhinological and Otolological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.
- Southern Surgical Association, Hot Springs, Va., Dec. 10-12. Dr. E. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
- Western Surgical Association, Topeka, Kan., Dec. 6-7. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery 10:125-156 (Oct.) 1940

- Chancroid, Granuloma Inguinale and Lymphogranuloma Venereum: Laboratory Aids and Problems in Diagnosis. E. S. Sanderson, Augusta, Ga.—p. 125.
Acute Cholecystitis and Biliary Disease: Immediate and Delayed Treatment: Report of Sixty-Two Cases. D. C. Donald, Birmingham.—p. 129.
Vomiting: Its Symptomatology. J. M. Bell, Mobile.—p. 135.
Pneumonia: Emphasis on Newer Forms of Treatment. R. O. Russell, Birmingham.—p. 138.

American J. Digestive Diseases, Huntington, Ind. 7:401-446 (Oct.) 1940

- Factors in Diagnosis of Intestinal Protozoa in Man and in the Interpretation of the Findings. J. L. Borland, Jacksonville, Fla.—p. 401.
*Acute Ulcerative Esophagitis. L. Bloch, Chicago.—p. 407.
Gastrointestinal Manifestations of Shock. P. Klemperer, A. Penner and Alice Ida Bernheim, New York.—p. 410.
Occurrence of Gastritis as Diagnosed by Gastroscoy in Gastric Neuroses. J. M. Ruffin and I. W. Brown Jr., with technical assistance of E. H. Clark, Durham, N. C.—p. 414.
Effect of Inflation of Stomach on Gastroscopic Picture. J. M. Ruffin and I. W. Brown Jr., with technical assistance of E. H. Clark, Durham, N. C.—p. 418.
Gastritis Simulating Peptic Ulcer. A. B. Rivers and L. A. Smith, Rochester, Minn.—p. 424.
Spontaneous Variations in Gastric Secretion in Response to Histamine Stimulation. W. L. Palmer, J. B. Kirsner and P. B. Nutter, Chicago.—p. 427.
Comparative pH Values Within the Stomach, Pylorus and Duodenum in Antacid Therapy. J. B. Eyerly, Chicago.—p. 431.
Correlation of Antral and Bulbar Pressures with Fluoroscopic Observations During Gastric Evacuation. J. P. Quigley, J. M. Werle and D. Brody, Cleveland.—p. 434.
*Secretin Test in Diagnosis of Pancreatic Diseases: Report of 130 Tests. J. S. Diamond and S. A. Siegel, introduction by J. L. Kantor, New York.—p. 435.
Presence of Spirochetes in Human Gastric Mucosa. A. S. Freedberg and L. E. Barron, Boston.—p. 443.

Acute Ulcerative Esophagitis.—Bloch discusses twenty-six cases of acute ulcerative esophagitis found at necropsy. Twenty of the cases were in adults and six in infants. In infants the condition may be due to thrush or to a complication of a congenital lesion, such as esophageal narrowing. The ages of the adults were between the third and the eighth decades; six of the patients were in the seventies. Six were men and fourteen women. Fourteen had been operated on, ten for disorders of the gastrointestinal tract. Of the non-surgical patients two died of acute coronary occlusion, one of congestive heart failure and hypertension, one of granulocytopenia with acute tracheobronchitis, one of carcinoma of the pancreas with duodenal invasion and one of subphrenic abscess and gastric ulcer complicating prostatic disease. The frequent association of peptic ulcer with acute ulcerative esophagitis has been observed by other workers. Little is known about the etiology of acute esophagitis. Butt and Vinson believe that the trauma produced by an indwelling Levin tube for decompressing the abdomen or irritation from vomiting are important causes. Intubation was done in eleven of seventeen cases of the present series in which operation was performed. Seven vomited and five, after intubation, vomited. It is not unreasonable to accept vomiting and intubation as a causative factor in the production of acute esophagitis. However, vomiting is extremely common postoperatively but acute esophagitis is comparatively rare. Penner and Bernheim believe that the same cause, the mechanism of shock, is responsible for the production of postoperative acute esophagitis, gastritis, duodenitis and colitis. In the present series at least

eleven patients who were operated on suffered from what might well be considered shock. One of the patients, following a gastric resection, showed not only acute esophagitis but acute membranous gastritis, duodenitis and colitis. Again many patients died of shock, but acute esophagitis did not develop in them. Other etiologic factors undoubtedly play a part. Embolism and thrombosis are favored by the presence of large venous channels in the lower end of the esophagus. The nervous system also must be considered. One of Bloch's patients had syphilitic meningo-encephalitis, another acromegaly and a third acute fulminating encephalitis. In contrast to chronic esophagitis there seems to be no way of diagnosing the acute type. Vomiting or regurgitation of blood stained fluid or the obtaining of such fluid through a tube should arouse the suspicion of its presence. Here the question arises whether vomiting is a symptom of or the cause of the esophagitis. Unfortunately, when acute esophagitis is present the underlying and primary condition is extremely serious. There is no special form of therapy for this type of case.

Secretin Test for Pancreatic Diseases.—Diamond and Siegel performed 130 secretin tests on 104 individuals; twenty-four were normal subjects and included physicians, students and others with unrelated ailments, and eighty were patients having such conditions as cholelithiasis, pancreatitis, obstructive jaundice, pancreatic cysts, steatorrhea, diabetes, hepatic cirrhosis with syphilis and ulcerative colitis. The test supplied the authors with valuable information of disturbed function of the gland in chronic states that had been unrecognized and unsuspected. In cholelithiasis with common duct stones the pancreas became simultaneously affected, revealing various degrees of disturbed function. In obstructive lesions when the pancreatic duct is encroached on from growths in the proximity of the duct the test supplied diagnostic data through a diminished or totally absent response, depending on the extent of blockage of the duct. In syphilis the test seemed to show a depressed function of the pancreas. This likewise occurred in cirrhosis of the liver, chronic alcoholism, acute yellow atrophy of the liver and the graver forms of toxic hepatitis. In the steatorrheas the test was most valuable in indicating the presence of pancreatic deficiencies and helped to differentiate between the idiopathic group including sprue and those with pancreatic lesions. In follow-up studies of the steatorrhea group the test showed the reversibility of the function and was consistent with the clinical improvement of the patient, indicating the degree of recovery.

American J. Obstetrics and Gynecology, St. Louis 40:545-726 (Oct.) 1940. Partial Index

- Development of Implantation Theory for Origin of Peritoneal Endometriosis. J. A. Sampson, Albany, N. Y.—p. 549.
More Recent Conceptions of Pelvic Architecture. W. E. Caldwell, H. C. Moyle and D. A. D'Esopo, New York.—p. 558.
Changing Conceptions of Ovarian Tumors. H. C. Taylor Jr., New York.—p. 566.
Certain Outstanding Trends in Gynecology During the Past Forty Years. R. T. Frank, New York.—p. 574.
Evaluation of Treatment of Uterine Cancer. W. P. Healy, New York.—p. 578.
*Puerperal Infection. B. P. Watson, New York.—p. 584.
Twenty Years of Progress in Endocrine Studies of Reproduction. C. F. Fluhmann, San Francisco.—p. 609.
Development of Maternal Welfare Activities. F. L. Adair, Chicago.—p. 633.
Vulval and Vaginal Mycosis and Trichomoniasis. H. C. Hesselstine, Chicago.—p. 641.
Increase in Hospital Deliveries. E. D. Place, Iowa City.—p. 659.
*Evaluation of Androgenic Therapy in Gynecologic Practice. J. W. Huffman, Chicago.—p. 675.
Clinical Experiences with Equine Gonadotropic Hormone. H. W. Erving, Christine Sears and J. Rock, Brookline, Mass.—p. 695.
Laboratory and Clinical Experience with Oral Pregnenolone. M. R. Cohen and I. F. Stein, Chicago.—p. 713.

Puerperal Infection.—Watson summarizes the advances in knowledge gained about puerperal infection in the last twenty years as follows: 1. Recognition of the part played by the anaerobes in puerperal and postabortal infection. 2. Proof that these anaerobic infections are endogenous in origin. 3. Proof that shock, hemorrhage, prolonged labor and traumatization of tissue predisposes to such infections. 4. Realization that the removal of dead and decomposing material resulting from this type of infection can, in most instances, be effected with no

risk, and usually with great benefit to the patient. 5. Identification of the different groups of the beta hemolytic streptococcus and proof that only group A is virulent in the human subject. 6. Establishment of the fact that infection with this organism is practically always exogenous. 7. Proof that these organisms are usually conveyed to the patient by a carrier who harbors them in the mouth, nose or throat. 8. Demonstration of the fact that the risk of infecting patients is practically nil by periodic nose and throat culture of all the members of the obstetric staff and of carriers, and complete masking of the nose and mouth of those attending the parturient and puerperal woman. 9. Demonstration of the persistence for long periods of the organisms in the environment of an infected individual even after she is removed from it. 10. A recognition of the necessity for complete isolation of all such infected women. 11. The discovery of the beneficial effects of sulfanilamide and its derivatives in streptococcal, gonococcal and *Bacillus coli* infections.

Androgenic Therapy in Gynecologic Practice.—Huffman reviews the experimental work and the clinical results obtained with androgen therapy in gynecology and states that the effects among twenty-two women who received androgenic therapy parallel those produced in laboratory animals by injections of testosterone propionate. Functional uterine bleeding was inhibited by the preparation. No notable masculinizing changes developed, except occasional temporary hypertrophy of the clitoris. Three patients have been under observation for more than two years. Testosterone propionate caused genital activity to cease in human beings as it has in the adult female rabbits and rats. This effect is the result of pituitary rather than ovarian inactivation. The changes produced are temporary, and the cyclic phenomena of the genitalia are resumed after administration of the drug is continued. When from 350 to 500 mg. of testosterone propionate is injected over a considerable period of time, temporary masculinizing changes, especially hypertrophy of the clitoris, may appear. Inhibition of lactation after testosterone propionate therapy has been observed clinically and microscopically in animals. According to the literature, reproduction is possible and normal children have been born to women who have been treated with the preparation prior to their pregnancies. There is considerable evidence to suggest that androgenic therapy has a place in the treatment of functional uterine bleeding, mastalgias, puerperal breast engorgement and inhibition of lactation. Further investigation of its use in dysmenorrhea and menstrual molimina is indicated. The use of the preparation may perhaps be advantageous in preference to the estrogens in certain menopausal disturbances.

American Journal of Psychiatry, New York

97:255-512 (Sept.) 1940

- Naval Psychiatric Problems. D. G. Sutton, Washington, D. C.—p. 255.
Chronic Rheumatic Brain Disease as Possible Factor in Causation of Some Cases of Dementia Praecox. W. L. Brutsch, Indianapolis.—p. 276.
Treatment of General Paresis with Malaria Induced by Injecting a Standard Small Number of Parasites. P. Hoch, E. Kusch and L. T. Coggeshall, New York.—p. 297.
Respiratory Plateaux in "Day Dreaming" and in Schizophrenia. W. Corwin, Waltham, Mass., and H. Barry, Tufts College, Mass.—p. 308.
Attempt to Delineate by Orderly Procedure Clinical Findings in So-Called Dementia Praecox (Schizophrenia). B. Cohen, North Grafton, Mass., and B. H. Flower, Boston.—p. 319.
Prognostic Criteria in Hebeephrenia: Importance of Age, Sex, Constitution and Marital Status. B. S. Gottlieb, New York.—p. 332.
Differential Diagnosis of Schizophrenia in Light of Concept of Personality Stratification. O. Kant, Worcester, Mass.—p. 342.
Improvement in Convulsive Therapy with Metrazol by Premedication with Scopolamine Hydrobromide. J. V. Edlin and E. S. Klein, Chicago.—p. 358.
Study of Central Action of Metrazol. B. Libet, J. F. Fazekas and H. E. Himwich, Albany, N. Y.—p. 366.
Paroxysmal Auricular Fibrillation Complicating Metrazol Shock Therapy. M. H. Hoffmann, N. Sandler and H. Hecht, Eloise, Mich.—p. 372.
Insulin Shock Treatment: Death Due to Pulmonary Gangrene. W. Furst, Norristown, Pa.—p. 380.
Effect of Alcohol on Cerebral Metabolism. W. Goldfarb, K. M. Bowman and J. Wortis, New York.—p. 384.
Psychometric Performance of Children Receiving Amphetamine (Benzedrine) Sulfate. C. Bradley and Emily Green, East Providence, R. I.—p. 388.
Child Psychiatry at Maudsley Hospital. E. Mildred Creak, London, England.—p. 395.

American Journal of Public Health, New York

30:1159-1268 (Oct.) 1940

- The Problem of Back Flow Preventive Measures Employed at the New York World's Fair. R. J. Gleason, New York.—p. 1159.
Responsibility of Organized Medicine in Medical Care. K. Emerson, New York.—p. 1171.
Typing of Typhoid Bacilli in Western States by Means of Bacteriophage. A. S. Lazarus, Denver.—p. 1177.
Rapid Methods for Estimation of Air Dustiness. H. H. Schrenk, Pittsburgh.—p. 1183.
Rapid Methods for Determination of Gases in Air. F. A. Patty, New York.—p. 1191.
The Problem of Malaria Mortality. H. W. Brown, Chapel Hill, N. C.—p. 1199.
Further Observations on Rapid Phosphatase Test. H. Schärer, New York.—p. 1206.
Incentives and Methods in Health Education, Adult Level, Medical Society View. R. H. Greenman, Rochester, N. Y.—p. 1211.
Diet and Resistance to Infection: III. Genetic versus Dietary Factors. C. F. Church and Claire Foster, Philadelphia.—p. 1217.
Civil Service in Public Health. C. F. Blankenship, San Francisco.—p. 1221.
Industrial Nursing: Supplementary Report of Study Committee on Industrial Nursing on Five Small Industries in Philadelphia County. Ruth W. Hubbard, Philadelphia.—p. 1224.

American Journal of Surgery, New York

50:1-224 (Oct.) 1940

- Rupture of Quadriceps Tendon: Report of Three Cases. F. M. Conway, New York.—p. 3.
Fallacy of Conjoined Tendon: Etiology and Repair of Inguinal Hernia. S. A. Ziemann, Chicago.—p. 17.
Surgical Importance of Accessory Spleens: Report of Two Cases. E. B. Settle, Rock Port, Mo.—p. 22.
Operation for Greater Mobilization of Transversalis Fascia in Repair of Direct Inguinal Hernias. W. F. Jones, New York.—p. 27.
Lobectomy for Bronchiectasis: Report of Two Cases. I. E. Siris, Brooklyn.—p. 29.
*Peripheral Arterial Embolism. J. J. Koucky, W. C. Beck and J. M. Hoffman, Chicago.—p. 39.
Closed Citrate Method of Collecting Blood. L. W. Diggs, Memphis, Tenn.—p. 50.
Glycerin Osmotic Drainage. E. D. Smith, Owensboro, Ky.—p. 55.
Factors Involved in Production of Adhesive Plaster Irritation. M. Grolnick, Brooklyn.—p. 63.
Use of Neosynephrin Hydrochloride in Maintaining Blood Pressure During Spinal Anesthesia. H. I. Silvers and I. E. Leonard Jr., Atlantic City, N. J.—p. 79.
Prevention and Treatment of Late Sequelae in Corrective Rhinoplasty. J. W. Malinac, New York.—p. 84.
*Treatment of Suppurative Generalized Peritonitis with Alcohol. R. J. Behan, A. B. Sigmund, W. Ruehl and J. A. Zewe, Pittsburgh.—p. 92.

Peripheral Arterial Embolism.—Koucky and his associates attempted to evaluate therapeutic measures in twenty-five cases of peripheral arterial embolism treated at the Cook County Hospital from 1928 to 1938. This probably does not represent all the cases, as many may have been filed under other diagnoses, remained unrecognized or cured spontaneously through the establishment of collateral circulation. Most cases of peripheral arterial embolism occur in late adult life. Two of the twenty-five patients were less than 10 years of age and two were between 70 and 80 years. As is usually observed, mitral heart disease, on the basis of subacute bacterial or chronic rheumatic carditis, was the direct etiologic agent. The lower extremities were more frequently involved than the upper. In the present series the ratio was 5:20. The treatment of arterial embolism is divided into four types: nonoperative, arteriotomy, arterectomy and amputation. An embolism to the upper extremity can usually be treated conservatively because the collateral circulation will furnish sufficient blood to the limb. Embolism of any large vessel in the lower extremity down to and including the popliteal arteries is a surgical emergency and should be treated as such without any hopeful procrastination. The time factor in the performance of an embolectomy is of great importance and one should not wait once the site of the embolus is reasonably certain. With procrastination, reformation of a thrombus at the site at which the embolus has impinged becomes an added risk to embolectomy. If a free flow of blood after the embolus is removed is impossible, it is best to remove a segment of the artery (arterectomy), thus removing the irritable focus of the vasospastic reflex and facilitating collateral circulation. From a review of the cases the authors have learned that the usual case follows a more or less typical course toward a fatal termination and that this course can be altered. The patient is brought to the hospital in poor general condition, conservative methods are employed, and he seems to rally and appears in a much better condition. Meanwhile the extremity becomes gangrenous. As

the patient improves he is kept on this conservative management for days or even weeks, appearing constantly to improve. Then there is a general increase in the toxemia. The fever rises, the pulse accelerates and a moderate leukocytosis gives evidence of toxemia. As this increases, the emergency guillotine amputation is performed. This is followed by shock, infection and death. The authors found that in cases in which amputation was done as soon as improvement was apparent the results were better. These amputations were far better borne and could be carried out as planned, elective procedures. The average duration of life of three patients following embolectomy was thirty-nine hours, of four of the six following amputation forty-seven days, and of fourteen of the sixteen given conservative treatment twenty days, a respective mortality rate of 100, 66 and 88 per cent.

Alcohol for Suppurative Generalized Peritonitis.—Behan and his co-workers have used since 1930 in all cases of peritonitis at operation intraperitoneal lavage with 70 per cent ethyl alcohol as a routine. If free fibrinous fluid or pus was found in the peritoneal cavity, a culture was taken and this was immediately followed by the introduction of from 100 to 200 cc. or more of 70 per cent ethyl alcohol into the abdominal cavity. The amount may be increased so that the walled off and localized abscess cavity is filled or, if a generalized peritonitis is present, so that the free peritoneal cavity is flooded. In generalized suppurative peritonitis the abdominal wall is elevated by retractors on either side of the incision and sufficient alcohol is introduced to fill the peritoneal cavity so that the fluid level is even with the margin of the incision. The alcohol remains in situ for a few minutes and is then siphoned off by suction. The usual complications of suppurative peritonitis (gastromesenteric ileus, paralytic ileus, tympany, persistent vomiting and hiccups) seldom occurred when this therapy was used. The authors believe the beneficial effect of alcohol due to its bactericidal action, reduction of bacterial activity, increase of resistance of all the tissues during this period, decreased absorption of toxins and poisonous tissue products during the period of reduced bacterial activity, induced hyperemia in the surface layers of the peritoneum and the beneficial systemic effect of the counter action of toxic products (because of inhibited absorption) in the circulation. The absorbed alcohol may act as a mild blood antiseptic and be a source of energy for the destruction of foreign proteins and other toxic substances, and it may also be of nutrient value because of its high caloric content. Forty-three cases of localized and forty-nine cases of generalized suppurative peritonitis were studied. Forty-six cases were treated by the alcoholic lavage of the abdominal cavity and the rest by wide incision and removal, if possible, of the diseased appendix. The majority of cases of acute suppurative appendicitis, localized appendical abscess and generalized suppurative peritonitis occurred in patients between 10 and 30 years of age. The average time of operation was about 4.23 days after the onset of the acute symptoms. The average period of delay before operation in cases in which alcohol lavage was used was 4.77 days and in the others 3.69 days. Patients treated with intra-abdominal alcohol lavage recovered more quickly than did those for whom alcohol was not used. In the alcohol treated group the temperature dropped to normal on an average, 9.1 days after operation, with the shortest period three days and the longest forty days (the latter case was complicated by postoperative intestinal obstruction). The average in the cases not treated with alcohol was 12.48 days. The shortest time in which the temperature returned to normal in this series was three days, the longest fifty-nine days. The pulse rate rose postoperatively to an average of 112 in the alcohol treated cases and to 127 in the other series. This may indicate that patients treated with alcohol did not remain so toxic. The average hospital time of the patients treated with alcohol was 22.04 days as compared to 27.59 days for those not so treated. The death rate in the series of generalized peritonitis treated with alcohol was 8.69 as compared to 45.39 per cent in the cases not treated with alcohol. The deaths were due to complications. There were no deaths among the cases of localized peritonitis. The prognosis was much better when culture of the intra-abdominal exudate showed a pure strain of organism than when it presented more than one organism.

American Review of Tuberculosis, New York

42:431-550 (Oct.) 1940

- *Artificial Pneumothorax: Résumé of Twenty Years' Experience. F. L. Jennings, Indianapolis; P. M. Mattill and Frances C. Nemecek, Oak Terrace, Minn.—p. 431.
- Leukocytic Counts in Tuberculosis: Comparative Study of Several Methods of Interpretation. E. M. Medlar, A. J. Lotka and M. Spiegelman, New York.—p. 444.
- *Instability of Tuberculin Reaction: Observations on Dispensary Patients, with Special Reference to Existence of Demonstrable Tuberculous Lesions and Degree of Exposure to Tubercle Bacilli. A. W. Dahlstrom, Philadelphia.—p. 471.
- Control of Tuberculosis: Factors Suggested by Statistics of Sanatorium Patients. J. G. Bohorfoush and Pauline E. Michael, Madison, Wis.—p. 488.
- Tuberculosis in Rabbits: Further Comparison of Roentgenologic and Pathologic Findings in Primary and Reinfection Experimental Pulmonary Tuberculosis in Rabbits: II. Reinfection Tuberculosis. H. E. Burke, New York.—p. 499.

Twenty Years' Experience with Artificial Pneumothorax.—For Jennings and his associates artificial pneumothorax has been for the last twenty years, and still is, the first choice among the various procedures used to collapse the lung. The method has the following advantages: 1. When satisfactory, pneumothorax collapses the diseased areas better than other methods. 2. It prevents the formation of pleural adhesions. 3. It can be augmented by other measures. 4. It may be discontinued with relative ease. It can never be predicted whether or not pneumothorax can be satisfactorily induced; only a trial will ascertain this. The authors think that, if such a trial does not establish collapse, other procedures should be used. They review the records of all patients for whom pneumothorax was considered suitable and who were discharged from Glen Lake Sanatorium prior to January 1937. There were 1,027 patients for whom unilateral pneumothorax was done or considered suitable. Among these there were 249 (24.2 per cent) who could not be given injections of air. Only a portion of the pleural space of 346 patients was found free from adhesions and the amount of pulmonary collapse was not sufficient to affect either the symptoms or the lesions. There were 111 patients who received some benefit from the air introduced into the pleural space. Either their symptoms were decreased or their lesions were partly controlled. There were 321 patients whose condition was classed as satisfactory because both their symptoms and their lesions were completely controlled by pneumothorax. Thus satisfactory collapse was obtained for only one out of every three patients. Follow-up examinations from one to twenty years revealed that patients who had the most satisfactory collapse and who had the greatest amount of free pleural space were in the best condition. Of patients not benefited by pneumothorax and subjected to further collapse, one out of four was dead three years from the time the pneumothorax was originally induced. Of those who had no other collapse procedures three out of four were dead. Further collapse constituted phrenic nerve surgery for 160 patients and thoracoplasty for fifty-four, while 125 had both phrenic nerve excision and thoracoplasty and seven patients had a combination of various procedures. These two groups of patients were treated over the same period of time in the same institution. Among 432 patients benefited by pneumothorax there were forty-eight who had phrenic nerve excision and ten who had intrapleural pneumonolysis. Thirty patients had phrenic nerve excision and thoracoplasty. Sixteen patients had a combination of various types of surgical collapse. Twenty-seven had thoracoplasty alone. Bilateral pneumothorax was induced or attempted 144 times. Seventy-six, or 52.8 per cent, of the patients are living and sixty-eight, or 47.2 per cent, are dead. Fifty of the sixty-eight deaths occurred within the first three year period. Bilateral pneumothorax is indicated for patients with active bilateral tuberculosis, for patients who develop tuberculosis in the contralateral lung during unilateral pneumothorax treatment and for patients whose tuberculosis becomes activated in the contralateral lung. A considerable number of the patients with bilateral pneumothorax underwent further surgery. The authors conclude that pneumothorax offers the best method of collapse when tuberculous lesions can be satisfactorily controlled by it. It shortens the period of bed rest.

Instability of Tuberculin Reaction.—Until recently an impression prevailed that, once established, the tuberculin reaction remained positive indefinitely. Dahlstrom points out that frequent discovery of calcified nodules, presumably of tuberculous origin, in patients not reacting to tuberculin has recently raised the question whether tuberculin allergy may not disappear after complete healing of the lesion and whether the allergy demonstrable in many cases of calcified lesions may not be dependent on chance reinfection rather than on the persistence of the original allergy. The question arises whether the tuberculin reaction, once established, remains positive during the activity of the lesion responsible for the initiation of allergy, in other words whether the tuberculin reaction is always positive in the presence of active tuberculous lesions. This study was undertaken to answer these questions and, in the event that the tuberculin reaction proved to be unstable, to determine the conditions under which allergy was maintained or lost. The dispensary records of 3,919 members of 513 families under observation from five to fifteen years were examined. Of these 2,490 were positive to tuberculin on at least one examination and 276, or 11.1 per cent, passed from the positive to the negative state during the period of observation. The lower the original degree of sensitiveness the greater was the likelihood of reversal from positive to negative. Only 0.4 per cent of 1,090 people giving a 3 plus reaction to the standard first dose of tuberculin became tuberculin negative, whereas the negative state supervened in 70 per cent of 185 persons giving a 1 plus reaction to the second dose. The greater the degree of family exposure the more likely was the reaction to remain positive. In families with no history of tuberculosis in any member 24 per cent of the members became negative, whereas among sixty-three reactors in families in which a patient with positive sputum resided constantly only one person (1.6 per cent) became negative. The tuberculin reaction never became negative in the group under consideration in the presence of lesions of active reinfection type tuberculosis but became negative in a small number of cases of tuberculous lesions of the type diagnosed only by x-ray examination. Reactive capacity disappeared in 0.72 per cent of the total number of patients with recognizable tuberculous lesions. The overwhelming majority of the unstable reactors were children. Reversion to negative reaction proved rare in adult life.

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- *Studies in Blood Preservation: Stability of Plasma Proteins. J. Scudder, New York.—p. 502.
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- Fluid, Salt and Nutritional Balance in Patients with Intestinal Suction Drainage. G. C. Penberthy, J. L. Irvin and R. M. Tenery, Detroit.—p. 530.
- Clinical Study of Plasma Volume in Acute Intestinal Obstruction. J. Fine, A. Hurwitz and J. Mark, Boston.—p. 546.
- *Plasma Loss in Severe Dehydration, Shock and Other Conditions as Affected by Therapy. A. S. Minot and A. Blalock, Nashville, Tenn.—p. 557.
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- Hypoproteinemia and Its Relation to Surgical Problems. I. S. Ravdin, Philadelphia.—p. 576.
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- *Gastric Acidity Before and After Operative Procedure, with Special Reference to Role of Pylorus and Antrum: Preliminary Report of Clinical and Experimental Study. O. H. Wangenstein, R. L. Varco, L. Hay, S. Walpole and B. Trach, Minneapolis.—p. 626.
- Diagnosis and Surgical Management of Leiomyomas and Leiomyosarcomas of Stomach. F. H. Lahey and B. P. Colcock, Boston.—p. 671.
- Abdominal Neoplasms of Neurogenic Origin. H. K. Ransom and E. B. Kay, Ann Arbor, Mich.—p. 700.
- Use of Intramuscular Injections of 2-Methyl-1, 4-Naphthoquinone in Treatment of Prothrombin Deficiencies, with Note on Role of Liver in Response to This and Other Substances with Vitamin K Activity. W. D. Andrus and J. W. Lord Jr., New York.—p. 783.

Blood Preservation.—Scudder obtained refrigerated plasma samples of varying ages from three different blood banks in New York City, unrefrigerated samples from Salisbury, N. C., plasma from the necropsy room of the Presbyterian Hospital and placental plasma from the Sloane Hospital for Women.

To ascertain what effect the lyophile process has on serum proteins, a sample of dried serum was supplied by Ravdin from Philadelphia. The electrophoretic method of analysis of proteins reported by Longworth and MacInnes was used. After a comparison of the values for preserved plasma with the values for fresh plasma in his studies and those of others, Scudder points out that the greatest change appears in the decrease of albumin as well as a change in the components which constitute the albumin/globulin ratio. Fibrinogen appears unaltered. A definite increase appears in the gamma globulin. This decrease in albumin and the increase in gamma globulin have been observed by Knoll. Two specimens which had been kept in a specially designed bottle showed the least change. In comparing the refrigerated samples with those that had been kept at room temperature and had been shipped about the country, the greatest difference was seen in the beta globulin fraction, the beta globulin disturbance was absent and the beta globulin/albumin ratio was decreased. The necropsy serum and plasma were abnormal. The placental plasma appeared within normal limits. The lyophilized serum presented an anomaly in that the beta disturbance was missing. It appears that postmortem blood is abnormal; this may not apply to blood collected from those who have died suddenly. Placental blood appears to be a normal source for conserved blood. Lyophilized serum appears abnormal. Refrigeration seems to enhance the preservation of plasma as did the shape of the flask. Possibly denaturation of plasma proteins is slower under these conditions.

Plasma Loss in Dehydration and Shock.—Minot and Blalock discuss the two factors vasodilatation and loss of circulating volume which lead to a deficiency of intravascular fluid and the measures for preventing and treating secondary or hematogenic shock. Under normal conditions many factors cooperate to maintain a fluid balance between the tissue cells and the extracellular spaces and in the vascular system. The fluid intake and electrolyte must keep pace with their loss from the body. There must be sufficient plasma protein to attract and hold an adequate volume of fluid in the blood stream. The selective permeability of the capillaries allows water and crystalloids to pass freely but withholds most of the protein in the blood stream. Renal activity removes metabolic waste products and any excess of fluid or electrolytes taken into the body. A serious abnormality in any of these factors may result in disastrous changes in the amount and partition of body fluid. Among the simpler abnormal conditions which may lead to a serious reduction in the volume of circulating blood are severe dehydration and extensive hemorrhage. In addition to these an abnormal partition of body water may arise from a nutritional lack of adequate plasma protein, as occurs in nutritional edema. Hypoproteinemia on a nutritional basis does not often lead to serious circulatory failure, but it must be corrected as it is a likely factor in the development of postoperative complications and some instances of pulmonary edema and pneumonia. Frequently an abnormal partition in body water occurs because the capillaries have been injured, permitting plasma protein, water and crystalloids to pass through the capillary endothelium into the tissue spaces. Mechanical, chemical or thermal trauma and oxygen lack are common causes of increased permeability of the capillaries. Although details of hematogenic shock vary with the condition initiating it, the problem of treating impending hematogenic shock is to restore and maintain a more effective circulation in the presence of the operative abnormalities. Attempts to increase vasoconstriction with drugs has failed as a means of preventing shock. More promising results were obtained from the administration of adrenal cortex extract, but still a large part of the treatment must be replacement of the elements lost from the blood stream. The difficulty of fluid replacement therapy varies with the different conditions, but the patient's needs for fluid and electrolytes must be met. Blood plasma has been most efficacious for fluid replacement. The introduction of aqueous solutions dilutes the plasma colloids in the blood stream and, if already low, further dilution prevents the retention of the administered fluid in the blood stream. Tissue edema develops while the blood stream remains dehydrated. If extensive capillary damage exists, the continuous adminis-

tration of fluid by vein washes out more protein and as a result may actually reduce rather than increase the volume of circulating blood. The best guide as to the disposal being made of intravenously administered fluid is afforded by frequent measurements of hematocrit or hemoglobin and of plasma protein. The use of plasma rather than of whole blood avoids further burdening of the circulation with cellular elements which are already present in high concentration. Volume for volume, plasma transfusions introduce protein approximately twice as fast as whole blood and there is less danger of reactions. The disadvantages of plasma are the technical difficulties and time required for preparing it for transfusion and the larger amounts of blood which must be furnished by donors. Therefore the value and convenience of an available "plasma bank" is evident. However, lacking plasma, transfusions of whole blood should be administered promptly and repeatedly. Many attractions are offered by desiccated or lyophilized blood serum. The dried powder can be kept indefinitely and be dissolved in a small volume of water, giving a solution richer in protein than fresh plasma. When whole blood or plasma cannot be procured, the blood volume may be restored by intravenous injections of acacia solutions.

Gastric Acidity Before and After Operations.—Wangenstein and his collaborators state that the surgical staff, while still adhering to orthodox indications for operative intervention, varied the surgical procedure with the thought of garnering useful information concerning the role of various operations in the management of ulcer and the manner in which their influence is mediated. In addition, experimental procedures have been carried out on the dog in an attempt to assay further the validity of Edkins's hypothesis of pyloric and antral hormone control of the gastric phase of gastric secretion. The occurrence of gastrojejunal ulcer in two cases in which antral resection had been done because of continued bleeding from a duodenal ulcer suggested this study. In both cases a previous gastro-enterostomy had been done and, when antral resection was performed, no evidence of a gastrojejunal ulcer was observed. In both cases gastrojejunal ulcer followed antral excision within a few months. Sixty cases in which the following types of operative procedure were done were available for study: (group 1) twenty-nine cases of retrocolic gastrojejunostomy, (group 2) six of antral excision with complete terminolateral anastomosis (Pólya), (group 3) ten of extensive gastric resection including pylorus and antrum, (group 4) six of antral excision with extensive gastric resection (Finsterer's operation) accompanied by either partial (Hofmeister) or complete retrocolic terminolateral anastomosis (Pólya), (group 5) three of Schmilinsky's operation with provision for complete intragastric regurgitation for gastrojejunal ulcer following antral excision, (group 6) five of tubular excision (fundus and corpus) with gastrojejunostomy, leaving the antrum and pylorus intact and (group 7) three of tubular excision (fundus and corpus) without gastrojejunostomy, leaving the antrum and pylorus intact. The postoperative observations made in these cases include studies of gastric acidity, gastric emptying time (employing the neutralization test) and gastric evacuation time determined fluoroscopically after the patient swallowed 150 cc. of a thin barium sulfate mixture. The authors found that: 1. Extensive gastric resection by itself does not produce achlorhydria to maximal stimulation (histamine), even when combined with bilateral subdiaphragmatic vagotomy (group 7). 2. Extensive gastric resection, when combined with gastrojejunostomy providing opportunity for partial intragastric regurgitation of duodenal content, will usually produce achlorhydria to maximal stimulation (histamine). The lapse of time is an important factor in the development of such achlorhydria. 3. Excision of the antrum and pylorus (the small or partial gastric resection) fails to make the residual gastric segment achlorhydric to maximal stimulation. 4. Allowing the antrum and pylorus to remain, as is indicated particularly by group 6, does not militate against securing an achlorhydric stomach to maximal (histamine) stimulation, granted that an extensive gastric resection of the acid secreting area is performed. Group 4 will, in time, shed additional light on this issue. 5. Gastrojejunostomy is not

accompanied by achlorhydria to maximal stimulation. 6. The emptying time is decreased considerably in all anastomotic operations on the stomach (groups 1, 2, 3 and 4) and after extensive resection of the stomach without anastomosis (group 7). When the intragastric regurgitation of the duodenal content is complete, as it is in group 5, the emptying time is prolonged (barium sulfate evacuation time). On the basis of their observations the authors conclude that the Edkins hypothesis on the clinical side appears to be invalid. Proof of this lies in two occurrences: the consistent production of true achlorhydria in five cases in which there was duodenal ulcer after tubular resection of the corpus and fundus (attended by gastrojejunostomy), leaving the pylorus and antrum intact (group 6) and failure to produce true achlorhydria in cases of excision of the pylorus and antrum (group 2). On the experimental side their observations are still incomplete except that excision of the pylorus and antrum does not decrease the secretory capacity of fundic pouches. The importance of the acid factor in ulcer is emphasized by the occurrence of ulcers in cats after intragastric instillation of 0.4 per cent hydrochloride and after subcutaneous intramuscular implantation of histamine in beeswax.

Archives of Internal Medicine, Chicago

66:785-1010 (Oct.) 1940

- *Observations on Induced Thiamine (Vitamin B₁) Deficiency in Man. R. D. Williams, H. L. Mason, R. M. Wilder and B. F. Smith. Rochester, Minn.—p. 785.
- Pain in Shoulder as Sequela to Myocardial Infarction. A. C. Ernestene and J. Kinell, Cleveland.—p. 800.
- Interauricular Septal Defect. W. S. Tinney Jr., Lancaster, Pa.—p. 807.
- Relative Significance of Concentration of Inorganic Sulfate in Serum and of Its Renal Clearance, with Special Reference to Diffuse Arterio-vascular Disease with Hypertension. A. Goudsmit Jr. and N. M. Keith, Rochester, Minn.—p. 816.
- Pancreatic Function in Case of Nontropical Sprue. Alice Childs and G. F. Dick, Chicago.—p. 833.
- Normal Blood Pressure. A. E. Trelor, Minneapolis.—p. 848.
- *Necrobiosis Lipoidica Diabetorum. Alice G. Hildebrand, H. Montgomery and E. H. Rynearson, Rochester, Minn.—p. 851.
- *Banti Syndrome (Fibrosclerotic Splenomegaly): Definition, Classification and Pathogenesis. P. Ravenna, Chicago.—p. 879.
- Gastro-Enterology: Review of Literature from July 1939 to July 1940. C. M. Jones, Boston.—p. 893.

Effect of Induced Thiamine Deficiency in Man.—

Williams and his associates confirm the observations of Williams, Mason and Smith by their own work, in which six subjects received a diet for eighty-eight days which provided less than 0.15 mg. of thiamine hydrochloride (50 international units of vitamin B₁) daily but which was otherwise adequate. After eleven days two of the subjects were given thiamine hydrochloride orally, without their knowledge, in gradually increasing daily doses. The four subjects who obtained no supplementary thiamine experienced striking evidences of nutritional deficiency. The two subjects whose diets were supplemented also showed evidences of deficiency until their total daily intake of the vitamin reached 0.95 mg. From then on they were free from symptoms and performed as effectively on a chest weight exercise machine as at the start of the study. With further increases of thiamine they improved still more, and when the daily intake reached 2 mg. they were strikingly more alert and attentive and their performance of the exercise was much more satisfactory than it had been originally. When the intake of thiamine was lowered by a return to the routine hospital diet, well-being, alertness and work performance again fell to the original level. This indicates that the institutional diet, which contained approximately from 0.6 to 0.8 mg. of thiamine hydrochloride daily, provided less than an optimal allowance. The food in this hospital compares favorably with that in most institutions and therefore institutional diets in general may be criticized on this score. The isolated withdrawal of thiamine from the diet did not produce beriberi. In the earlier study four subjects were given food that contained less than 0.15 mg. of thiamine daily for 147 days, and the four subjects of the present study received a diet that provided less than 0.15 mg. for eighty-eight days. Yet edema, cardiac dilatation and neuritic pain were absent in both groups. Mild tenderness of the muscles of the calves and paresthesia of the feet and legs and diminution of tendon reflexes were

observed. Pain to any degree was not present. The authors wonder whether thiamine is the vitamin the lack of which is responsible for the classic features of beriberi. They suggest that deficiency of the factors of the vitamin B complex other than thiamine may be more important in the production of such features than thiamine itself. The early stage of the condition induced by the restricted intake of thiamine closely resembled neurasthenia; the later stage simulated anorexia nervosa. The authors suggest that states of thiamine deficiency, as these exist in our part of the country, where few cases of beriberi or pellagra are encountered, should be looked for principally in cases rightly diagnosed as neurasthenia.

Necrobiosis Lipoidica Diabeticorum.—Hildebrand and her co-workers point out that since Oppenheim's description in 1929 of necrobiosis lipoidica diabeticorum seventy-eight cases have been reported, to which they add the eight encountered at the Mayo Clinic since 1936, when the first case was registered. In more than 87.2 per cent of all the cases diabetes mellitus has also been present, in a few instances the cutaneous lesions preceded the onset of diabetes by as long as eight years and among 10 per cent of patients with these lesions diabetes has not yet appeared. In those with diabetes the cutaneous lesions had developed from several months to as long as seventeen years after the onset of the diabetes. Aside from the high incidence of diabetes, study has failed to reveal the presence of any predominant associated disease which might have etiologic significance. All the patients were white and more than 80 per cent of them were women. The cutaneous lesions usually appeared when the patients were between 10 and 40 years of age, the average being 35 years. In the majority of the cases the diabetes has been poorly controlled throughout its course. Trauma seemed to play a definite part in the causation of the cutaneous condition, as from 12 to 16 per cent of the patients stated that bruises, cuts, scratches and mosquito bites preceded the necrobiosis. In approximately 85 per cent of all cases reported elsewhere and in 82 per cent of the authors' cases the lesions occurred on one or both legs below the knees. A diagnosis of necrobiosis lipoidica diabeticorum is possible on the clinical appearance of the lesions alone. The plaques are flattened with yellowish centers surrounded by violaceous or red-brown borders, with or without central ulceration. These lesions differ from other xanthomatoses, which are usually firm, yellowish papules occurring on the extensor surfaces of all four extremities. The intracellular deposit of lipoids in foam cells in the latter lesions makes recognition final. The pathogenesis of the condition remains obscure. Because of the vascular changes seen in the lesions, many authors have assumed that the disease is due to damage to the small blood vessels of the corium, possibly by circulating toxins, with subsequent thrombosis, necrosis and secondary imbibition of fat particles. Another hypothesis assumes a local lipid disturbance in the skin, based on a general disturbance in fat metabolism. Neither hypothesis has proved satisfactory. Treatment, either local or general, for most patients with diabetes mellitus has been of little avail. The cutaneous lesions typically run an indolent, chronic course, either slowly enlarging over a period of months or years or slowly receding to form depressed scars. Control of the glycosuria with proper diet and insulin seems to have little effect on them, although some authors have reported good results with diets low in fat. Three of the patients at the Mayo Clinic were placed on such a diet but no improvement occurred after they had been observed for from several months to a year. Local treatments, including injection of insulin at the site of the lesions, ultraviolet irradiation and various local medications, have been unsuccessful in accelerating healing.

Banti Syndrome.—According to Ravenna, accumulating evidence supports the view that Banti's splenomegaly is largely due to splenic congestion and that this congestion is not dependent on portal-venous obstruction. The congestion may be due to primary lesions of the small splenic arteries which regulate the blood flow into the spleen ("primary active congestion"). The human spleen should be considered an elastic rather than a contractile organ. Its variations in size depend on variations in the volume of inflowing blood rather than on

active contractions of the smooth muscle of its supporting framework. Mechanically the spleen might be defined as an automatic controller which regulates the pressure of the splenic venous blood in order to maintain the balance between the volume of inflowing blood and the amount which can be discharged through hepatic resistance. In pathologic conditions the splenic elasticity guarantees a pressure sufficient to secure the further progress of venous portal blood. Congestive splenic enlargement is therefore a mechanism to counterbalance either an increased volume of portal blood or an increased peripheral resistance to the discharge of a normal amount of blood. The Banti syndrome is a symptom complex dominated by chronic fibrocongestive splenomegaly, accompanied by portal hypertension and complicated by, or associated with, hepatic cirrhosis or thrombosis of the splenic and portal veins. It may depend on various determinable causative agents, either infective or toxic, or undeterminable ones. The splenic changes of the Banti syndrome are probably due to primary lesions of the splenic arterioles, the regulating power of which becomes insufficient to control the inflow of blood. The consequent congestive splenomegaly is the cause of the circulatory disturbance in the portal bed. Secondly, hepatic cirrhosis and venous thrombosis may aggravate the state of portal circulation.

Archives of Surgery, Chicago

41:813-1042 (Oct.) 1940

- *Experimental Studies on Headache: Pain Sensitive Structures of Head and Their Significance in Headache. B. S. Ray and H. G. Wolff, New York.—p. 813.
- Direct Inguinal Hernias: Study of 605 Hernias and 565 Repairs. H. J. Shelley, Fort Worth, Texas.—p. 857.
- Use of Serial Dilutions in Determination of Prothrombin by One Stage Technic. J. G. Allen, O. C. Julian and L. R. Dragstedt, Chicago.—p. 873.
- Localization of Staphylococci in Areas of Inflammation Produced by Xylene. R. H. Rigdon, Memphis, Tenn.—p. 879.
- *Cancer of Tongue. H. E. Martin, H. Munster and E. D. Sugarbaker, New York.—p. 888.
- Perforation as Complication of Gastric Carcinoma. M. A. Casberg, St. Louis.—p. 937.
- *Ischemic Contracture of Lower Extremity. T. Horwitz, Philadelphia.—p. 945.
- Factor of Bile Stasis in Experimental Production of Gallstones in Dogs. H. G. Aronson, Chicago.—p. 960.
- Cause of Death in Cases of Mechanical Intestinal Obstruction: Consideration of Certain Confused Issues and Review of Recent Literature. E. L. Besser, Iowa City.—p. 970.
- Acute Metastatic Spinal Abscess: Report of Two Cases with Recovery Following Laminectomy. D. L. Reeves, Los Angeles.—p. 994.
- A Soluble Rod as Aid to Vascular Anastomosis: Experimental Study. S. Smith, Chicago.—p. 1004.
- *Acute Pancreatitis: Etiologic Review and Report of Thirty-Five Cases. E. F. Lewison, Baltimore.—p. 1008.
- Lymph in Experimental Burns. G. O. Wood, Nashville, Tenn.—p. 1038.

Experimental Studies on Headache.—Ray and Wolff present data on the pain sensitive structures inside and outside the cranium obtained from 150 observations on thirty patients during operative procedures. The following conditions prevailed among the thirty patients: 1. Surgical exposure of cerebral lesions afforded an opportunity to make careful observations on the sensitivity to pain. 2. The patients were intelligent and cooperative, so that pain, its site and its nature could be determined. 3. The patients were relatively free of apprehension and of preoccupation with pain, requiring minimal analgesia. 4. The operative procedures were such that the patients were not prostrated or inarticulate and therefore could describe their sensations. 5. The stimulated structures were free of disease, insuring normal responses. Some of the "pain pathways" and mechanisms of headache after various stimuli were as follows: 1. The tissues covering the cranium are all more or less sensitive to pain, the arteries especially so. 2. Of the intracranial structures, the great venous sinuses and their tributaries from the surface of the brain, parts of the dura at the base, the dural arteries and the cerebral arteries at the base of the brain are sensitive to pain. 3. The cranium (including the diploic and emissary veins), the parenchyma, the dura, the pia-arachnoid, the ependymal lining of the ventricles and the choroid plexuses are not sensitive to pain. With the exception of sensations resulting from stimulation of the parenchyma and nerves, the only sensation of the intracranial structures was pain. Stimulation of the pain sensitive intracranial structures on or

above the superior surface of the tentorium cerebelli resulted in pain (pathways in the fifth cranial nerve) in various regions in front of a line drawn vertically from the ears across the top of the head; stimulation on or below the inferior surface resulted in pain behind this line. The pathways for this pain are chiefly in the ninth and tenth cranial and the upper three cervical nerves. From the data available, headache may result from (1) traction on the veins that pass to the venous sinuses from the surface of the brain and displacement of the great venous sinuses, (2) traction on the middle meningeal arteries, (3) traction on the large arteries at the base of the brain and their main branches, (4) distention and dilatation of intracranial and extracranial arteries, (5) inflammation in or about any of the pain sensitive structures of the head and (6) direct pressure by tumors on the cranial and cervical nerves. Intracranial diseases cause headache by involvement of more than one pain sensitive structure. Headache from intracranial disease is usually referred pain. Unilateral hyperalgesia localized in the parietal area may indicate a lesion near the middle meningeal artery, and hyperalgesia localized to the postauricular region a lesion about the internal auditory meatus.

Cancer of Tongue.—Martin and his associates studied the records of 556 consecutive patients with lingual cancer admitted to the Memorial Hospital during 1927 to 1934 inclusive. This series comprises all patients with microscopically proved lingual cancer except those observed for less than one month. At the Memorial Hospital lingual cancer comprises about 15 per cent of all tumors of the upper respiratory and alimentary tracts and about 25 per cent of all intra-oral tumors. The average age of the 556 patients was about 58 years at the time of admission; 87 per cent of the patients were men and 13 per cent were women. Chronic irritation was a predominating apparent etiologic factor in growths of the middle and anterior thirds of the tongue where precancerous changes, such as chronic diffuse or localized glossitis and leukoplakia, occur most often. At the base of the tongue, tissue changes as a result of chronic irritation are less definite. Such chronic irritation (leukoplakia, chronic glossitis and dental sepsis) are much more prevalent in men than in women, supporting the etiologic relationship of chronic irritation to intra-oral cancer. The chronicity of the irritant is more important than its nature. Single traumas probably have little effect. Routine Wassermann tests revealed that about 33 per cent of the patients had syphilis, in whom the immediate etiologic factor undoubtedly was the chronic glossitis of late syphilis. The influence of tobacco on lingual cancer is difficult to estimate; about 75 per cent of the male patients admitted moderate to heavy use of tobacco. This figure loses most of its significance, as even a higher percentage of the general adult male population uses tobacco. Only 9 per cent of the women admitted smoking. If only the nonsmokers of both sexes are considered, the disease is still more than twice as frequent in men as in women. In the sixth and seventh decades, when the incidence of intra-oral cancer is greatest, a large percentage of the general population has suffered dental diseases and defects for prolonged periods. However, their presence may be coincident with the "cancer age" rather than its direct cause. As with tobacco, dental factors render affirmation or denial impossible. Only 10 per cent of the patients had clean teeth in good repair. In clinic patients dental defects and sepsis were almost the rule. In a few instances the association of sharp, broken or worn teeth or ill fitting dentures with the growth is evident. The primary early small lesion was treated with radon seeds. Fractionated peroral roentgen irradiation supplemented by radon seeds was used for all except the small growths. Fractionated roentgen irradiation through the neck followed by supplementary radon seeds was used for cancer of the base of the tongue. Radon seeds ("overdosage") followed in from five to ten days by partial glossectomy was indicated for only a few bulky, fungating, partly necrotic tumors. The following variations were also employed: (1) roentgen irradiation for extremely radiosensitive tumors; supplementary interstitial irradiation being probably indicated in all cases, (2) low voltage, lightly filtered peroral roentgen irradiation for superficial growths on the anterior portion and dorsum of the tongue and (3) surgical

excision for fungating papillary tumors at the tip of the tongue. Complications following surgical procedures are apt to be acute and severe but of short duration; those following irradiation tend to be of lesser degree but of longer duration. Except in the earliest stages when the tumor is small and is situated on the edge of the anterior half of the tongue the prognosis of lingual cancer is bad. The average duration of life among the patients from the first symptom to death was twelve months, varying between two months and seven years when the immediate postoperative deaths are excluded. The five year end results of the 556 patients were as follows: Fifty-three patients without recurrence died of other causes. Five without recurrence were lost track of. Of the remaining 498, 368 died as a result of the cancer, two with a recurrence were lost track of and probably are dead, four are living with a recurrence of their cancer and 124 are free from lingual cancer five or more years after treatment. Thus a five year cure rate of 25 per cent obtains if the 124 successful results are divided by the determinate group of 498.

Ischemic Contracture of Lower Extremity.—Horwitz reports two cases of disabling deformities of the right lower extremity which persisted for eleven and fourteen years respectively. The two cases presented the following features: (1) healed fractures of the femur, (2) massive induration of the muscles of the leg and foot associated with atrophy and loss of motor power below the knee, (3) vascular dysfunction in the involved lower extremity, (4) contractural deformities of the foot and toes, (5) x-ray evidence of extra-osseous calcification of the leg and (6) histologic evidence in one case of massive degeneration of muscular tissue with fibrous tissue replacement and extensive calcification. In both cases the pathologic state in the lower extremity was identical with Volkmann's ischemic contracture. On the basis of his two cases and a review of eighteen cases reported in the literature the author concludes that such ischemic contracture must be anticipated after fracture or extensive injury to the soft tissues without fracture in the lower extremity, especially in the region of the knee and leg. The contracture and deformity may be avoided by fasciotomy during the acute (prodromal) stage. Deformities following contractures may be corrected by nonoperative and operative measures.

Acute Pancreatitis.—Lewison states that there were thirty-three cases of acute pancreatitis among 100,000 admissions between 1921 and 1939 to the Beth Israel Hospital. This incidence coincides with that reported by other investigators, but the author believes that its rarity may have been overestimated. Serum amylase and lipase studies indicate that acute pancreatitis may be mild and more prevalent than heretofore believed. In the milder form it may masquerade as biliary colic. The diagnosis of the thirty-three cases and two treated elsewhere was established or confirmed at operation. Cases of manifest chronic pancreatitis, acute pancreatitis secondary to primary processes elsewhere, acute pancreatitis resulting from perforation of a peptic ulcer and pancreatic calculi were not considered. The author points out that a consideration of its pathogenesis demonstrates a significant relation to organic diseases and to functional disturbances of the biliary tract. Etiologic agents incapable when acting individually of producing this disease may, when combined, assume a principal pathogenic role. Hemorrhagic, edematous, suppurative and gangrenous types of pancreatitis have been distinguished and each requires individual attention regarding diagnosis, prognosis, prophylaxis and treatment. There was a mortality of 17 per cent in the thirty-five operative cases of acute pancreatitis reported. Of these, 54 per cent were of type 1—acute edematous pancreatitis, a rather benign phase of the disease. Pain and tenderness, usually in the epigastrium or the upper part of the abdomen, were constant clinical observations. Radiation of pain to the back, vomiting and a history of similar recurrent attacks were elicited frequently. Incision and drainage of the pancreas combined with one or more ancillary procedures was carried out in 77 per cent of the cases. Use of the serum amylase test as an aid in diagnosis may tend to modify conservatively the future surgical treatment of acute pancreatitis.

Indiana State Medical Assn. Journal, Indianapolis

33:499-602 (Oct.) 1940

- Recent Outbreak of Poliomyelitis in Indiana. V. K. Harvey and T. B. Rice, Indianapolis.—p. 499.
- Sodium Sulfapyridine: Its Chemotherapeutic Action and Toxicity. H. M. Powell and K. K. Chen, Indianapolis.—p. 503.
- Statistical Analysis of 1,700 Sudden and Violent Deaths. W. E. Kruse, Fort Wayne.—p. 509.
- Acute Perforative Appendicitis. M. B. Welborn, Evansville.—p. 517.
- Fractures of Neck of Femur: General Consideration of Some Methods of Treatment and Special Reference to Use of the Two-Plane Direction and Range Finder of Engle and May. J. S. Robison, Winchester.—p. 520.
- Gastric Anemia Syndromes. M. Sandorf and M. Davidhoff, Indianapolis.—p. 523.

Johns Hopkins Hospital Bulletin, Baltimore

67:229-308 (Oct.) 1940

- Current Bronchopneumonia of Unusual Character and Undetermined Etiology. Y. Kneeland Jr. and H. F. Smetana, New York.—p. 229.
- Bronchopneumonia of Unknown Etiology (Variety X): Report of Thirty-Two Cases with Two Deaths. W. T. Longcope, Baltimore.—p. 268.

Bronchopneumonia of Unknown Etiology.—Longcope describes the clinical course of the infection variously called atypical pneumonia, pneumonitis and bronchopneumonia. There is evidence of its contagiousness and it may be extremely severe. For convenience he designates the disease "bronchopneumonia, variety X". During the last few years he has observed thirty-two completely investigated cases. The ages of the patients ranged from 17 to 70 years. Seventeen were between 20 and 30 years of age. Twenty of the patients were men, eleven of whom were doctors, medical students, orderlies or hospital employees. Twelve of the patients were women and seven of these were nurses. The disease occurred at all seasons of the year, though eighteen cases were encountered during October, November and December. Ten cases occurred from May to September inclusive. Pneumococcic pneumonia is most prevalent in Baltimore from December to May, a period during which only eight of the cases under discussion were encountered. The incubation period is from about fourteen to twenty-one days. Usually the acute phase of the disease was preceded by a day or two of malaise with a rasping and nonproductive cough, and then fever accompanied by increasing cough, headache, general aches and discomfort, chilly sensations and occasionally abdominal pain and nausea. Only six of the thirty-two patients had an actual chill at onset. Five complained of pain in the chest, which was not sharp or stabbing and was rarely affected by respiration. Two had epistaxis as an early symptom. Four had pharyngitis due to beta hemolytic streptococci accompanying the onset of the disease. When the patients were first seen, often on the first to the third day of their illness, the temperature varied from 102 to 105 F. Usually the pulse rate and respiration were not proportionately elevated. The patients did not appear or feel very ill. The most annoying symptom was the rasping, nonproductive cough. Sometimes there was a small amount of sputum, which in a few instances was blood tinged but not rusty. The throat was sometimes reddened. The lungs during the first few days of illness usually showed no conspicuous abnormality, though a few patients presented a slight dullness over one or the other lower lobes, with suppressed breath sounds and a few fine rales over this area. A common characteristic of the disease in the early stages was a moderate leukopenia. The onset of the disease was similar in most cases, but the subsequent course varied from a mild infection to extreme gravity or fatality. The study throws no light on its etiology. Blood cultures made, often repeatedly, in twenty-seven of the cases gave no growth. The occasional occurrence in the sputum of a few nonpathogenic pneumococci which could not be typed can have little significance. The appearance of hemolytic staphylococci in the sputum during the latter stages of the disease in two cases suggests that secondary infections by pathogenic bacteria may occur. No serious attempt was made to isolate a filtrable virus, but experiments to accomplish this with the solidified lung in one of the two fatal cases resulted in failure. The reported results of such work by Reimann and by Francis and Magill are of uncertain significance, and the experience of Kneeland and Smetana shows that if a filtrable virus is the cause of the disease it has not been definitely identified. However, many features of the disease suggest a

filtrable virus. These are its contagiousness, the long incubation period, the inability to demonstrate any known pathogenic bacteria and the peculiarity of the pathologic pulmonary changes, for the exudate in the alveoli has been found to consist largely of mononuclear cells. The clinical features of the disorder appear sufficiently distinctive to allow one, even without knowledge of its etiology, to recognize the infection as a disease entity. Significant features for such an assumption are its characteristic onset, the prolonged persistence of symptoms and signs, the migration of the pulmonary lesions from one lobe to another, the biphasic elevation in temperature and the appearance of many fine, coarse or explosive rales during convalescence.

Journal of Allergy, St. Louis

11:537-652 (Sept.) 1940

- Antigenic Relationship of Cotton Linters, Dust and Dust Precursors. E. J. Coulson and H. Stevens, Washington, D. C.—p. 537.
- *Electrolyte and Water Exchange in Bronchial Asthma, with Emphasis on Influence of Pitressin. A. V. Stoesser and M. M. Cook, Minneapolis.—p. 557.
- Note on Serum Sodium Concentrations of Allergic and Nonallergic Persons. P. B. Donovan and G. F. Harsh, San Diego, Calif.—p. 567.
- Study in Food Allergy: Relationship Between Allergic Activity and Protein Fractionization of Selected Foods. J. J. Engelfried, Ann Arbor, Mich.—p. 569.
- Studies on Colloidal Gold Phenomena in Allergy. M. H. Grow and H. A. Stiff, Dallas, Texas.—p. 578.
- The Future of Allergy: Presidential Address. W. T. Vaughan, Richmond, Va.—p. 584.
- Poison Oak and Poison Ivy: I. Dermatit Unit as Standard Measure of Potency for Extracts from These Plants. E. K. Stratton, San Francisco.—p. 591.
- Susceptibility to Poison Ivy Dermatitis. L. Zisserman, Philadelphia.—p. 600.

Electrolyte and Water Exchange in Bronchial Asthma.—Stoesser and Cook observed a group of children with persistent bronchial asthma in whom certain changes in the electrolyte and water balance caused definite variations in the degree of asthma. Placing the patients on a special low mineral, acid-ash diet which induced a low water retention improved the asthmatic condition, and subsequent artificial fever often caused the asthmatic symptoms to disappear. The remissions brought about by these procedures could be terminated by adding sodium chloride to the special diet or returning the patients to the general hospital diet, which was without salt restriction. During the periods of such diets artificial fever produced no consistent favorable influence on the asthma. These observations led the authors to determine the relationship between the electrolyte and water balance in the mechanism of asthmatic attacks. Pitressin offered a means of determining whether the increased water storage or the extra salt was instrumental in precipitating the symptoms. Pitressin, when injected subcutaneously, causes a retention of body fluids without the aid of an increase in body salts. Many asthmatic children were given pitressin, and six of them with intractable asthma who tolerated it were subjected to special studies. A total of twenty observations was made. The subjects were placed on an extremely low sodium chloride diet, and when pitressin was administered some retained as much as 2 Kg. (4½ pounds) of water. The asthma began to improve during the antidiuretic phase and continued through the diuretic and subsequent periods, proving that the storage of large amounts of water in the body and its sudden loss had little influence on the asthmatic symptoms. A review of the literature shows that during pitressin antidiuresis and diuresis, despite a low salt intake, sodium chloride is excreted, leading to a marked loss of body salt. It appears that bronchial asthma can be ameliorated, even in the presence of excessive hydration, if an associated depletion of sodium chloride exists. The authors draw no conclusions but point out that the study is of value as an investigative tool rather than a therapeutic procedure.

Journal of Aviation Medicine, St. Paul

11:101-140 (Sept.) 1940

- Experimental Study on Effect of Noise on Gastric Secretion in Pavlov Dogs. P. E. Vaughan and E. J. Van Liere, Morgantown, W. Va.—p. 102.
- Intra-Ocular Pressure at High Altitudes. E. A. Pinson, Dayton, Ohio.—p. 108.
- The Primary Flight Phase: Psychobiologic Consideration of Early Instruction in Flying. H. B. Porter, Washington, D. C.—p. 112.

Journal of Experimental Medicine, New York

72:331-548 (Oct.) 1940

- Infection of Guinea Pigs by Application of Virus of Lymphocytic Choriomeningitis to Their Normal Skins. H. J. Shaughnessy and J. Zichis, Chicago.—p. 331.
- Depressor Effect of Splenorenopepy on Hypertension Due to Renal Ischemia. D. M. Weeks, A. Steiner, J. S. Mansfield and J. Victor, New York.—p. 345.
- Studies on Sensitization of Animals with Simple Chemical Compounds: VIII. Sensitization to Picric Acid: Subsidiary Agents and Mode of Sensitization. K. Landsteiner and A. A. Di Somma, New York.—p. 361.
- Prolonged Coexistence of Vaccinia Virus in High Titer and Living Cells in Roller Tube Cultures of Chick Embryonic Tissues. A. E. Feller, J. F. Enders and T. H. Weller, Boston.—p. 367.
- Soluble Antigen of Lymph III. Dependence of Antisubstance Antibodies, and Role of Soluble Antigen to Infection. J. E. Smadel and M. J. Wall, New York.—p. 389.
- Studies of Murine Strain of Poliomyelitis Virus in Cotton Rats and White Mice. C. W. Jungblut and M. Sanders, New York.—p. 407.
- Use of Ultraviolet Light in Preparing Nonvirulent Antirabies Vaccine. H. L. Hodes, L. T. Webster and G. J. Lavin, New York.—p. 437.
- Influence of Age Factors on Susceptibility of Mice to Rabies Virus. J. Casals, New York.—p. 445.
- Influence of Age Factors on Immunizability of Mice to Rabies Virus. J. Casals, New York.—p. 453.
- Nutritional Cytopenia in Monkeys Receiving Goldberger Diet. P. L. Day, W. C. Langston, W. J. Darby, J. G. Wahlin and Virginia Mims, Little Rock, Ark.—p. 463.

Journal of Lab. and Clinical Medicine, St. Louis

26:1-286 (Oct.) 1940. Partial Index

- Autonomic Nervous System Considered in Relation to Experimental and Clinical Phenomena. D. E. Jackson, Cincinnati.—p. 4.
- Interaction of Vitamins and Drugs with Cell Catalysts. F. Bernheim, Durham, N. C.—p. 20.
- Clinical Laboratory Determination of Vitamin Nutrition. H. Field Jr. and D. Melnick, Ann Arbor, Mich.—p. 45.
- Role of Blood Clotting Anomalies in Hemorrhagic Diseases. J. H. Ferguson, Ann Arbor, Mich.—p. 52.
- Preserved Blood "Banks" in Relation to Transfusion in Treatment of Disease. J. A. Kolmer, Philadelphia.—p. 82.
- *Treatment of Allergic Disorders with Histamine and Histaminase. H. L. Alexander, St. Louis.—p. 110.
- Possible Significance of Inhibitory Effect of Fever on Anaphylactic Phenomena. P. de Kruif, Holland, Mich., and W. M. Simpson, Dayton, Ohio.—p. 125.
- Serology of Syphilis. R. L. Kahn, Ann Arbor, Mich.—p. 139.
- Takata-Ara Test in Liver Disease. T. B. Magath, Rochester, Minn.—p. 156.
- Some Chemical Observations on Human Heart in Health and Disease. V. C. Myers and G. H. Mangun, Cleveland.—p. 199.
- *Functions of Carotid and Aortic Bodies. C. F. Schmidt, Philadelphia.—p. 223.
- Epilepsy: Newer Methods of Investigation and Treatment. W. G. Lennox, Boston.—p. 232.
- Medical Problems of High Altitude Flying. H. G. Armstrong and J. W. Heim, Dayton, Ohio.—p. 263.

Histamine and Histaminase for Allergic Disorders.—

According to Alexander, evaluation of the therapeutic efficacy of histamine and histaminase for allergic disorders must be tentative for the present. Reported experience shows a rather striking similarity between the clinical effectiveness of the two. Neither appears to be of value for extrinsic allergy as asthma and hay fever, in which an immunologic mechanism is involved. Both are effective in urticaria, angioneurotic edema and physical allergy; that is, intrinsic allergy. This suggests that histamine operates through the production of histaminase. That intrinsic allergy responds to it and the extrinsic form does not leads to the question whether the H substance released by the one is qualitatively the same as that elaborated on contact between allergen and antibody. The question whether H substance is really histamine has been raised frequently and there are indications that the two are not identical. The limiting of histamine and histaminase therapy to intrinsic allergy, which is by far the more intractable type, shows sufficient promise to warrant further investigation.

Functions of Carotid and Aortic Bodies.—Schmidt reviews the knowledge of the functions of the carotid and aortic bodies. The function of these structures is to respond to changes in the chemical composition of the arterial blood by setting up afferent impulses which enter the central nervous system with the glossopharyngeal and vagus nerves, respectively. These impulses are stimulant to the medullary centers (respiratory, vasomotor and, in the case of the carotid body of the dog, cardio-inhibitory). The impulses from the stretch receptors of the carotid sinuses and aortic arch are inhibitory

to these centers (except the cardio-inhibitory, which is stimulated by them). The chemically sensitive receptors (chemoreceptors) can be stimulated by anoxemia, asphyxia, increased carbon dioxide tension or increased hydrogen ion concentration or by a variety of drugs and poisons. Reflexes from these structures are responsible for much, if not all, of the stimulant effects of anoxia on respiration and circulation. They probably are not concerned in the normal control of respiration unless the centers are depressed, in which event these reflexes become an important factor in maintaining respiration. An explanation that is in accord with existing information is that the chemoreceptors represent a survival in a relatively undifferentiated form of a reflex mechanism originally developed for a water-breathing ancestral form. The ability of these structures to set up a strong reflex stimulation to respiration when exposed to an environment that would depress or paralyze nerve cells (severe anoxia, high carbon dioxide tension or acidity, deep narcosis) is probably related to their primitive status and responsible for much, if not all, of their value to the organism.

New England Journal of Medicine, Boston

223:523-560 (Oct. 3) 1940

- Protrusion of Lower Lumbar Intervertebral Disks. W. J. Mixter and J. S. Barr, Boston.—p. 523.
- Acute Surgical Emergencies of Abdomen in Pregnancy. J. A. Smith and M. K. Bartlett, Boston.—p. 529.
- Severe Hemorrhage from Head and Neck: Its Management, with Report of Case Showing Retroparotid Space Syndrome. H. L. Albright, Boston.—p. 532.
- Clinical Management of Breast Tumors. G. W. Taylor, Boston.—p. 538.
- Rocky Mountain Spotted Fever: Analysis of Seven Cases, Including One Laboratory Infection. E. P. Campbell, Philadelphia, and W. H. Ketchum, Washington, D. C.—p. 540.
- Urologic Surgery: Urethral Catheter. W. C. Quinby, Boston.—p. 543.

223:561-606 (Oct. 10) 1940

- *Weil's Disease in the United States: Report of Case in Connecticut. F. G. Blake, New Haven, Conn.—p. 561.
- Advances in Roentgen Ray Treatment of Tumors of Bladder. F. H. Colby and R. Dresser, Boston.—p. 565.
- Rib Joints. J. E. Goldthwait, Boston.—p. 568.
- Primary Echinococcal Cyst of Uterus. M. L. Welcker, G. D. Kaneh and R. H. Goodale, Worcester, Mass.—p. 574.
- Mental Problems of Mid Life: Review of 100 Cases. C. T. Prout and A. U. Bourcier, Arlington Heights, Mass.—p. 576.
- Thoracic Surgery. E. D. Churchill, Boston.—p. 581.

Weil's Disease in the United States.—Blake points out that since 1935 sporadic cases of Weil's disease have been recorded with increasing frequency in the United States. In five of these the diagnosis seems to have been adequately supported by confirmatory laboratory tests, namely successful transmission of the infection to guinea pigs, demonstration of *Leptospira icterohaemorrhagiae* at necropsy or the development of specific agglutinins to a titer of 1:30,000. A number of other, less well documented, cases have been reported. The author cites the clinical history of a man aged 29 who, on Nov. 11, 1939, was suddenly seized with pain in the calves of both legs, weakness and dizziness. He developed chills, fever and headache and his neck became stiff and painful. He was nauseated and vomited frequently. His physician sent him to the hospital on the morning of November 12. On admission the patient appeared acutely ill, bathed in perspiration, pale, weak and apprehensive. The conjunctivas were injected, the lips and tongue were dry. The neck was stiff and painful. The lungs showed a few moist rales. The blood pressure was 96 systolic, 68 diastolic. There was tenderness of the abdominal muscles. The liver and spleen were not felt. All deep reflexes were slightly hyperactive. The abdominal reflexes were lacking. The Kernig test was negative. The white cell count was 27,350. A lumbar puncture showed an initial pressure of approximately 250 mm. of water. The fluid had a cell count of 30 per cubic millimeter, mostly red blood cells; a Pandy test was negative; a culture showed no growth. Blood cultures showed no growth. Agglutination tests for typhoid, paratyphoid and brucellosis were negative. The predominant symptoms during the first four days were prostration, fever, headache, meningismus and severe myalgia, principally in the neck, back and legs. On the third day epistaxes began, recurring at intervals until the thirteenth day. A second lumbar puncture on the fourth day revealed a clear spinal fluid under

normal pressure with 80 red blood cells per cubic millimeter. On the fifth day moderate jaundice developed; it lasted about a week. The liver became palpable and tender. From the tenth day on, the patient steadily improved. He was discharged on the nineteenth day for further convalescence at home, no diagnosis having been established. After returning home the patient again developed headache and soreness in the legs. His appetite was poor, and he felt drowsy and feverish. His vision seemed slightly blurred, and he vomited. On the twenty-seventh day of his illness he was again admitted to the hospital. A few days after admission, review of the clinical course of the illness suggested Weil's disease. The patient stated that about ten days before the onset of his disease he had been engaged in tearing down an old barn which was swarming with rats. Dark field examination of the urinary sediment, possibly too late for a positive result, failed to reveal leptospirae, but samples of blood serum collected on the thirty-eighth and forty-seventh days were reported to show complete agglutination with type 1 *Leptospira icterohaemorrhagiae* to a dilution of 1:10,000 and 1:30,000, respectively. Taken in conjunction with the history of exposure to rats, an appropriate incubation period and the typical course of the illness, the positive agglutination tests seem adequate to establish the diagnosis of Weil's disease. The author concludes that the more frequent recognition and diagnosis of Weil's disease depends on a wider appreciation of its prevalence, a greater familiarity with its clinical symptomatology, particularly that of the initial preicteric stage, and a more frequent use of laboratory tests of proved diagnostic value.

New Orleans Medical and Surgical Journal

93:169-222 (Oct.) 1940

- Functional Uterine Bleeding. W. Long, Oklahoma City.—p. 169.
Conservative Care of Acute Pyosalpinx in Young Women. B. C. Garrett, Shreveport, La.—p. 175.
The Elderly Primipara. J. S. Herring, New Orleans.—p. 177.
General Discussion of the Problems of Old Age. I. L. Robbins, New Orleans.—p. 184.
Nervous and Mental Aspects of Old Age. T. A. Watters, New Orleans.—p. 187.
Medical Treatment of the Aged. A. Eustis, New Orleans.—p. 193.
Surgery in the Aged. I. Cohn, New Orleans.—p. 196.
Medicine as a Vocation. Shirley C. Lyons, New Orleans.—p. 199.
Reconstruction Operations for Fracture of Neck of Femur with Nonunion. R. H. Aldredge, New Orleans.—p. 201.
Surgery in Treatment of Pulmonary Tuberculosis. P. R. Gilmer, Shreveport, La.—p. 208.

Surgery, Gynecology and Obstetrics, Chicago

71:409-568 (Oct.) 1940

- *Malignant Melanomas: Report of Four and Seven Year Cures. J. B. Brown and L. T. Byars, St. Louis.—p. 409.
Pathologic Physiology of Joints. H. Kelikian, Chicago.—p. 416.
*Congenital Atresia of Extrahepatic Bile Ducts. N. F. Hicken, Salt Lake City, and H. G. Crellin, Pittsburgh.—p. 437.
Superiority of Neocarphenamine and Sulfathiazole in Therapy of Staphylococcus Aureus Infections in Marrow Cultures. E. E. Osgood, Julia Joski and Inez E. Brownlee, Portland, Ore.—p. 445.
Hydration of Hyperthyroid Patients and Its Relationship to Edema, Especially Cerebral. W. Bartlett Jr., St. Louis.—p. 450.
*Primary and Secondary Neurilemmoma of Bone. D. A. DeSanto and E. Burgess, New York.—p. 454.
Comparison of Irving and Pomeroy Methods of Tubal Sterilization. Frances Hill Fox, Boston.—p. 462.
Nervous Factor in Traumatic Shock. V. Lorber, H. Kabat and E. J. Welte, Minneapolis.—p. 469.
New Valvular Cholecystogastrotomy. J. A. Glassman, Chicago.—p. 478.
Surgical Treatment of Unequal Leg Length. P. H. Harmon, Sayre, Pa., and W. M. Krigsten, Sioux City, Iowa.—p. 482.
Diverticula of Urinary Bladder: Clinical Study of 236 Cases. H. L. Kretschmer, Chicago.—p. 491.
Oblique Muscle-Cutting Incision in Acute Appendicitis. J. H. Saint, Santa Barbara, Calif.—p. 504.
Treatment of Trimalleolar Fractures of Ankle. M. C. Nelson and N. K. Jensen, Minneapolis.—p. 509.
Carcinoma of Breast: Report of 418 Cases Treated at St. Luke's Hospital from 1922 to 1933. B. R. Shore, New York.—p. 515.
Omphalocele (Umbilical Eventration) in the Newborn. R. E. Gross and J. B. Blodgett, Boston.—p. 520.
Use of Tourniquet in Removal of Tumors in Posterior Mediastinum. W. D. Andrus, New York.—p. 528.

Malignant Melanomas.—Brown and Byars state that nearly every one has pigmented moles and that not all of them should be or need be removed. The safest procedure is to destroy all moles that are subjected to chronic irritation whether they are pigmented or not. Every lesion that shows evidence of growth, increase in vascularity, change of color, repeated infection or ulceration should be removed, as should be the smooth coal-black

nevi. The developmental mole that appears at any time during life and progresses in size is probably the type that most often becomes malignant. The removal of moles should be quick, painless, nonirritating and thorough and should involve minimal handling of the growth. The change from an innocent pigmented nevus to a malignant one should not be difficult to detect and diagnose. Early signs are an increase in elevation or surface area, deepening of pigmentation, increase in vascularity and an apparent chronic infection with slight tenderness. A new localized process in the skin or under the nail presenting an increase in bulk and lacking the pain and tenderness of an infection and the characteristics of a wart should be considered as a malignant neoplasm. Obvious melanin may not be present. Death almost never occurs from extension or erosion of malignant melanomas of the face and head, as may be the case in other malignant conditions of the face. This is probably due to the fact that hopeless metastases and death occur so rapidly. Treatment is limited to surgery, as melanomas are resistant to radiation. The surgical procedure should remove a generous margin of normal surrounding skin and the underlying subcutaneous tissue down to the fascia, and sometimes it may be necessary to sacrifice a facial nerve or the full thickness of the cheek. Melanomas require the earliest possible widespread removal to avoid metastasis; as to the time element in metastasis, one might almost compare hours in melanomas to weeks in other carcinomas following treatment of the local lesion. There are five possibilities: 1. The initial lesion may recur following removal or remain cured. 2. Metastases may occur in the adjacent skin varying from uniformly deeply pigmented velvety areas to stippled smutty patches. This is probably a precursor of widespread metastases. 3. The most hopelessly swift spread is the sudden appearance of skin metastases in many parts of the body, with or without evidence of visceral involvement. 4. The local lesion may remain cured but later, from a few months to twenty-five years, the patient may die of a visceral metastasis. 5. This group contains those cases in which the primary focus is eradicated and the metastasis appears in the regional lymph nodes and is held in check for some indefinite period. Radical block dissection of the neck has shown definite promise and gives the patient his only chance for life. If the primary lesion is located so that its lymph drainage is fairly predictable, a prophylactic dissection should be done. Eleven cases of malignant melanomas are cited. One of the patients has survived for seven, three for four years and the others only up to one and a half years.

Congenital Atresia of Extrahepatic Bile Ducts.—During the last five years Hicken and Crellin encountered five cases of congenital atresia affecting the biliary radicles and have devised an x-ray method to visualize the abnormal biliary tract at the time of operation, thus giving the surgeon a concept of the problem that confronts him. Corrective surgery which establishes a new channel for the flow of bile into the intestinal tract, thus decompressing the liver, offers the only hope of cure. It has been held that these cases were hopeless but recent studies indicate that from 20 to 30 per cent are amenable to surgery. The method of visualizing the ductal deformities at the time of operation employed by the authors is contrast roentgenography as used on adults to obtain exact anatomic patterns of the tract while the patient is on the operating table. These cholangiographic studies proved helpful in visualizing and locating the obstructive lesions affecting the diminutive biliary tract of the infant. The cholangiograms not only facilitated the classification of the obstructions but greatly aided the surgeons in selecting the proper remedial procedure.

Primary and Secondary Neurilemmoma of Bone.—That nerve sheath tumors frequently originate in bone and periosteum is well attested by occasional communications in the literature. There is a form of nerve sheath tumor the specificity of which is assured by a distinctive microscopic appearance and clinical behavior, which unfortunately is referred to by a variety of names (peripheral neurinoma, peripheral neuroma, neurofibroma, perineural fibroblastoma, schwannoma and recently by Stout as a neurilemmoma) indicating a diversity of opinion as to its histogenesis. In spite of an extensive survey of the literature dealing with this condition DeSanto and Burgess found only a

single brief reference by Gross, Bailey and Jacox to the undoubted occurrence of this tumor in bone. Peers described a cystic tumor located in the mid shaft of the ulna that would now be classified as a neurilemmoma. The prevalent concept that once a neurogenic tumor invades bone it is highly malignant and the possibility of cure is practically nil is fallacious and often leads to needless sacrifice of an extremity. The authors report two cases which showed extensive osseous destruction yet were undoubtedly benign. They do not intend to imply that malignant neurogenic sarcomas of bone do not occur. Every case must be decided on its own merits. Mere bone invasion by a neurogenic tumor is by itself inadequate to insure the diagnosis of a malignant tumor. The authors' first case is similar to the cases reported by Gross, Bailey and Jacox and by Peers in anatomic and x-ray appearance. They involved the mid shaft region of the bone, replacing portions of cortex and medullary cavity. The tumor found by Gross and his associates was removed by local excision, whereas DeSanto and Burgess treated the tumor by resecting a portion of the ulna. Finger-like processes of tumor tissue extended into the cortical bone in such a fashion as to leave doubt that simple excision would have proved adequate. Their second case was nonencapsulated and invaded the sacrum, indicating that occasionally the tumor may be locally invasive. Indeed, it even infiltrated the ligamentum flavum. Because of its location, complete removal was not possible and recurrence is anticipated. X-ray examination was done in both cases and cystic lesions with punched out cortical rarefactions were revealed in the first case. Neurilemmoma of bone is not to be confused with the less specific neurofibromas of bone in association with systemic and skeletal manifestations of von Recklinghausen's disease.

Surgery, St. Louis

8:575-738 (Oct.) 1940

- *Partial Gastrectomy for Peptic Ulcer: Review of Seventy-Four Operations. R. D. McClure and L. S. Fallis, Detroit.—p. 575.
- Transpleural Esophagogastrostomy for Carcinoma of Esophagus and for Carcinoma of Cardiac Portion of Stomach: Report of Two Cases. B. N. Carter, Jean Stevenson and O. A. Abbott, Cincinnati.—p. 587.
- Regulation of Circulation in Different Postures. E. Asmussen, E. H. Christensen and M. Nielsen, Copenhagen, Denmark.—p. 604.
- Tumor Embolism of Common Femoral Artery, Treated by Embolectomy and Heparin. K.-E. Groth, Uppsala, Sweden.—p. 617.
- *Aneurysm of Splenic Artery. L. Sperling, Minneapolis.—p. 633.
- *Cavernous Hemangioma of Spleen. F. L. Cole and J. H. Forsee, Washington, D. C.—p. 639.
- Further Studies of Hemorrhage and Serum Infusion. F. Neuwelt, S. O. Levinson, W. Olson and H. Necheles, Chicago.—p. 644.
- Subdiaphragmatic (Perirenal) Extension of Staphylococci Empyema. V. A. Weinstein, New York.—p. 648.
- Experiments with Tampons and Membranes Made of Collagen. H. Feriz, Amsterdam, Netherlands.—p. 654.
- Solitary True Diverticulum of Cecum: Report of Case. J. C. Owings and Z. Morgan, Baltimore.—p. 662.
- Congenital Hourglass Bladder. N. F. Ockerblad and H. E. Carlson, Kansas City, Mo.—p. 665.
- Viability of Testis Following Complete Severance of Spermatid Cord. H. Neuhoef and W. H. Mencher, New York.—p. 672.
- Bifurcation Operation. H. Milch, New York.—p. 686.
- Apophysal Intervertebral Joints. A. Oppenheimer, Beirut, Syria.—p. 699.

Partial Gastrectomy for Peptic Ulcer.—McClure and Fallis analyze the records of seventy-four consecutive partial gastrectomies performed for peptic ulcer which did not yield to medical treatment. The results justify the continuance of partial gastrectomy which removes from two thirds to three fourths of the stomach. The mortality for the group was 5.3 per cent and all deaths were due to peritonitis. No death has occurred among the last thirty-four patients in the series. The men outnumbered women nine to one. More than one half of the patients had submitted to previous operations on the gastrointestinal tract. Pain, and nausea and vomiting were the most constant symptoms, being present in 85.2 and 70.2 per cent of the patients, respectively. Roentgenograms were the greatest single aid to diagnosis. Among more than 90 per cent of the cases the x-ray observations were corroborated at operation. The ratio of duodenal to gastric ulcer was two to one, whereas the ratio among the authors' perforated ulcer series was three to one. One of the four patients who died did so after early postoperative complications developed; all survived late complications. The end result was excellent or good among 75 per cent of the patients. Carcinoma, suspected neither clinically

nor at operation, was diagnosed by the pathologist in five cases. The authors attribute their decrease in the mortality rate to improved operative technic resulting from increased experience and to the adoption of such measures as spinal anesthesia, routine blood transfusions during operation, continuous gastric suction in the postoperative period and oxygen during and immediately after the operation to avoid anoxia and to lessen the occurrence of pulmonary complications.

Aneurysm of Splenic Artery.—Literature contains record of only eleven cases of aneurysm of the splenic artery with survival after operation, according to Sperling, who cites a case in which this condition was considered preoperatively and recovery followed splenectomy and removal of the aneurysm. The pathologic report was that of a calcified arteriosclerotic aneurysm of the splenic artery. The classic x-ray picture described by Lindboe was present, leading to a correct preoperative diagnosis. Seven cases were found in the 33,810 necropsies performed at the University of Minnesota up to January 1939. Less than 100 cases have been recorded since the report of Crisp in 1847.

Cavernous Hemangioma of Spleen.—Cole and Forsee report what they believe to be the first successful outcome of a rupture of a cavernous hemangiomatous spleen, mistakenly diagnosed as acute appendicitis. Emergency splenectomy, performed seventeen hours after the onset of symptoms, proved successful. Hemangioma of the spleen is either a capillary or a cavernous primary vascular tumor. The first consists of a formation of dilated vascular channels in the splenic tissue which gradually become converted into tubules. In the cavernous type the capillary system is lost and the hemangioma consists of a series of freely intercommunicating spaces of varied sizes, lined with endothelium. They are usually considered congenital. Usually the symptoms of benign hemangiomatous spleen are of long duration and are characterized by a gradually increasing tumefaction in the left hypochondrium, associated with pain, loss of weight and anemia. Surgery is the only curative therapy, and splenectomy is necessary. The twenty-two previously reported cases of benign hemangioma of the spleen are tabulated.

Wisconsin Medical Journal, Madison

39:797-896 (Oct.) 1940

- Treatment of Upper Respiratory Tract Infections in Children. H. K. Tenney, Madison.—p. 816.
- Gangrene in Diabetes. A. H. Beard, Minneapolis.—p. 821.
- Lymphogranuloma Venereum: Report of Thirty-Three Cases. A. G. Schutte, Milwaukee, and J. M. Lubitz, Wauwatosa.—p. 823.
- Practical Problems of a Physician with a Combined Obstetric and Pediatric Practice. H. A. Siscoek, Superior.—p. 827.
- Early Diagnosis of Pulmonary Tuberculosis in General Practice. R. H. Stiehm, Madison.—p. 831.

Yale Journal of Biology and Medicine, New Haven

13:1-160 (Oct.) 1940

- Studies on Fowl Leukosis: Transfer with Fractions Obtained by Ultracentrifugation of Leukemic Plasma and Bone Marrow Extracts. A. Kirschbaum, K. G. Stern and C. W. Hooker, New Haven, Conn.—p. 1.
- Studies on Relation of Kidney to Cardiovascular Disease: II. M. C. Winternitz and R. Katzenstein, New Haven, Conn.—p. 15.
- Actions of Colchicine and of Ethylcarbamylamine on Tissue Cultures. R. Tennant and A. A. Liebow, New Haven, Conn.—p. 39.
- Effect of Colchicine and X-Rays on Transplantable Mammary Carcinoma in Mice. J. W. Hirshfeld, R. Tennant and A. W. Oughterson, New Haven, Conn.—p. 51.
- Neutralization of Tumor Viruses by Blood of Normal Fowls of Different Ages. F. Duran-Reynals, New Haven, Conn.—p. 61.
- Hemorrhagic Disease Occurring in Chicks Inoculated with Rous and Fujinami Viruses. F. Duran-Reynals, histopathologic findings by R. M. Thomas, New Haven, Conn.—p. 77.
- Production of Degenerative Inflammatory or Neoplastic Effects in New-born Rabbit by Shope Fibroma Virus. F. Duran-Reynals, New Haven, Conn.—p. 99.
- N-Methyl and N-Dimethyl Substituted Sulfanilamides: Synthesis and Pharmacologic and Therapeutic Properties. R. A. Lewis and M. Tager, New Haven, Conn.—p. 111.
- Hydrogen Ion Concentration of Cerebral Cortex in Relation to That of Arterial Blood. C. Marshall and L. F. Nims, New Haven, Conn.—p. 117.
- Cardiovascular Effects of Potassium, Calcium, Magnesium and Barium: Experimental Study of Toxicity and Rationale of Use in Therapeutics. A. W. Winkler, H. E. Hoff and P. K. Smith, New Haven, Conn.—p. 123.
- Cortical Representation of Taste in Man and Monkey: II. Localization of Cortical Taste Area in Man and Method of Measuring Impairment of Taste in Man. W. S. Bönstein, New Haven, Conn.—p. 133.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Experimental Pathology, London

21:161-242 (Aug.) 1940

- Simple Culture Medium for General Use Without Meat Extract or Peptone. G. P. Gladstone and P. Fildes.—p. 161.
Experiments on Growth in Vitro of Virus of Yellow Fever. G. M. Findlay and F. O. MacCallum.—p. 173.
Immunization Experiments with Artificial Complexes Formed from Substances Isolated from Antigen of Bacterium Shigae. S. M. Partridge and W. T. J. Morgan.—p. 180.
Relationship of Lesions of Suprarenal Gland to Diphtheritic Toxemia. E. Holmes and H. Lehmann.—p. 196.
Observations on Lymphocytes in Tissue Culture. J. Medawar.—p. 205.
Observations on Lymphocytes in Chambers in Rabbit's Ear. R. H. Ebert, A. G. Sanders and H. W. Florey.—p. 212.
Enzymic Activity of Vaccinal Elementary Bodies. M. G. Macfarlane and D. E. Dolby.—p. 219.
Latent Carcinogenic Action of 3:4-Benzpyrene; Results of Intermittent Applications to Skin of Mice. S. Beck and P. R. Peacock.—p. 227.
Spontaneous Disintegration of Certain Blood Pigments, with Special Reference to Methemalbumin Formation. N. H. Fairley.—p. 231.

British Journal of Ophthalmology, London

24:469-540 (Oct.) 1940

- Dystrophies of Macula. A. Sorsby.—p. 469.
Note on Genetic Aspects of Macular Dystrophies. H. Gruneberg.—p. 530.

British Journal of Radiology, London

13:325-356 (Oct.) 1940

- Tomography of Spine and Sternum. M. Weinbren.—p. 325.
Double Radium Mold Treatment of Carcinoma of Floor of Mouth and Lower Alveolus. A. G. G. Melville.—p. 337.
Some Geometric Methods of Projecting Dose Contours. C. W. Wilson.—p. 345.
Tuberculosis of Stomach. A. E. Connolly.—p. 351.
Simple Method for Use of Standard Stereoscopic Radiographs in Plane Differentiation. E. D. Gray.—p. 354.
Suprasternal Bones Demonstrated in the Living Subject. H. Morris.—p. 356.

British Medical Journal, London

2:405-436 (Sept. 28) 1940

- *Plea for More Local Operation in Really Early Breast Carcinoma. D. C. L. Fitzwilliams.—p. 405.
*Tuberculosis of Knee Joint in Adults. L. A. Key.—p. 408.
*Testosterone Propionate in Functional Impotence. A. W. Spence.—p. 411.
March Fracture: Report on Case Involving Both Feet. R. Drummond.—p. 413.
Removal of Teratomatous "Twin." V. Pennell and L. C. Martin.—p. 414.
Benign Cyst of Parotid Gland. M. G. Kini.—p. 415.
Glomus Tumor, with Observations on Variations of Pain with Temperature: Case. J. D. N. Nabarro.—p. 416.

Local Operation for Early Breast Carcinoma.—Fitzwilliams presents data to show that local excision of really early mammary cancer is justifiable. He defines an early carcinoma as one in which there is a faintly perceptible something in the breast—hardly a lump and certainly not a tumor. These tumors have one invariable characteristic: they throw a shadow on strong transillumination. If such a shadow is seen, nine times out of ten the tumors will be carcinomatous. Strong transillumination is the only method of diagnosing them. Of ninety-three patients suitable for the conservative procedure five were lost track of, sixty-two are living and twenty-six are dead. Of the five patients lost track of one went to Argentina the same year, one was lost sight of after eight years and one was known to have kept well for one year and eight months, one for three years and three months and one for nine and a half years. Of the sixty-two living patients forty-seven had no recurrences. The longest survival among these forty-seven patients is fourteen and a half years. Twelve patients have lived longer than ten years and eighteen between five and ten years. Of the fifteen living patients who have recurrences, three have distant but no local manifestations and twelve have local recurrences. The average survival time of these patients has been ten and one half years, varying from two years and eight months to nineteen years. Recurrences appeared locally in an average of two years and nine months. Of the patients who died, twelve did so of intercurrent disease, eleven died of carcinoma but without local recurrence and three died after local recurrence but not necessarily because of it.

The survival time of these twenty-six patients ranged from six months to twenty-four years. The average survival was more than six years. The author points out that casual observation of many of the patients would not have disclosed the fact that the breast had been operated on. After operation constant vigilance on the part of the doctor, and the willing cooperation of the patient, are necessary. The author's contention is that local operation in really early cases of mammary cancer can confer the same amount of safety as the more extensive operation.

Tuberculosis of Knee Joint in Adults.—Key discusses the general aspects of the tuberculous knee joint. All but nine of 108 patients treated at St. Luke's Hospital, Lowestoft, from 1931 to 1935 have been followed up recently. Of these patients 37.75 per cent had tuberculous lesions elsewhere. History of trauma, probably bearing some relation to the development of the tuberculous joint, was elicited in 15 per cent of the cases. The average interval from the injury to the onset of symptoms was four and a half months. By the time the diagnosis is made, pathologic changes in a tuberculous knee joint have passed the earlier stages of disease. This was the fact in 87 per cent of seventy-seven cases of recently developed osseous disease, increasing subsequently to 96.1 per cent. Focal osseous disease by itself undergoes three principal changes: 1. The disease remains comparatively localized and reaches quiescence; bone cavities become obliterated or remain circumscribed by well calcified bone. 2. The disease extends laterally and causes abscess formation in the soft tissues. 3. The diseased area extends downward. This is the most common occurrence, and once the joint becomes grossly infected the later destructive changes progress until quiescence is eventually established. In repair fibrosis is the predominant factor. Pain is the first symptom in 70 per cent of cases. Swelling of the joint with pain or stiffness is present in 54 per cent of patients when medical advice is first sought. In a further 22 per cent the initial abnormality noticed by the patient was a swelling of the knee. Limitation of movement is gross and is accompanied by spasm when the joint surfaces are eroded. Tenderness, when present, is most often elicited on the inner side of the joint. Local warmth is always present. Abscess formation in the early stage of the disease occurs in 6.5 per cent. X-ray changes in the early tuberculous knee joint are usually inconclusive. One or more of the following abnormalities are usually seen: (1) general haziness, (2) increased width of the soft tissue shadow, (3) osteoporosis, (4) diminished joint space and (5) lack of definition or thinning of the cortical bone. After an average interval of four months from the onset of symptoms an abscess cavity or cavities are usually present in bone; localized marginal erosion may also be seen. Destructive osseous changes are more advanced than they appear on x-ray examination. Early diagnosis is difficult. It is justifiable to treat an obscure case of subacute arthritis as potentially tuberculous until proved otherwise. The insidious onset of joint symptoms is important, as is their spontaneous alleviation, which is never complete. The patient's general physical condition is an untrustworthy guide, as in 87 per cent it is good or only slightly deteriorated. Bacteriologic examination of pus from an abscess is the most valuable laboratory aid. Biopsy of the synovial membrane is inadvisable. In adults, tuberculosis of the knee joint may be confused with subacute chronic infective or gonorrheal arthritis, syphilis, hemophilia, traumatic lesions and neoplasms. Conservative treatment is indicated when the disease is purely synovial, when the bone focus or foci are removed from the articular margin and are surrounded by healthy bone, in quiescent cases with widespread osseous involvement and when other active tuberculous lesions exist. Conservative treatment appeared to suffice for only thirty cases. Thirty-one of the 108 patients returned to the hospital, indicating that free movement or bony ankylosis should always be sought. Arthrodesis, after arrest of the general illness and local disease, is the best treatment for most cases. Active septic infection of sinuses and persistently active local disease are its chief contraindications. Bony union was obtained in 83 per cent of fifty-nine cases. The five cases in which firm fibrous ankylosis resulted have remained functionally excellent, but the result must be regarded as having fallen short of the objective.

Two incomplete fibrous unions and three nonunions (two of which subsequently required amputation) were chiefly due to operating when the disease was active. Three of the ten patients having amputations died within a few days of operation, three survived operation and left the hospital but have died at varying intervals since, and four patients are well. Amputation is a last resort, but the tendency is to delay it too long. A patient suffering from profound toxemia has often passed the stage when amputation could have saved his life. Widespread disease may exist with remarkably little constitutional disturbance and amputation should not be performed until prolonged conservative treatment has failed to give any sign of recovery.

Edinburgh Medical Journal

47:585-644 (Sept.) 1940

Edinburgh Medical School a Hundred Years Ago. R. Thin.—p. 585.
Modern Therapy in Specific Infections. R. C. L. Batchelor.—p. 601.
Acute Leukemia: Clinical and Hematologic Study. A. Piney.—p. 616.
*Carcinoma of Stomach in Young Subjects. J. G. Macleod and R. B. Baird.—p. 627.

Carcinoma of Stomach in Young Subjects.—Macleod and Baird state that ten cases of gastric carcinoma in persons 30 or less years of age occurred among 700 cases of carcinoma of the stomach treated since 1934 at the Royal Infirmary, Edinburgh. Some of the observations in these cases differ from those reported by other workers. Six of the ten cases occurred in women, in contrast to Bruckner's report that men were affected twice as often as women. Microscopic confirmation was obtained in six cases, and the tumors in four were adenocarcinomatous, one scirrhous and one medullary. The pyloric antrum of eight was involved, the lesser curvature of one and the whole of the stomach of one. No particular disease, certainly not peptic ulcer, was simulated, and the characteristic course (in seven cases) commenced with a period of vague dyspepsia in which abdominal pain was a common feature. All this is contrary to the observations of Bruckner. Vomiting was present in nine cases; it tended to occur later and to be of an obstructive type. Pyrexia was uncommon, being persistent in only one case. A mass, far from being infrequent, was palpable in seven cases. This is in keeping with the observations of Phillips in that in those cases in which the tumor was measurable it was greater than 6 cm. in diameter at operation of 73.6 per cent of the patients. In keeping with Bruckner's observations the average duration of symptoms prior to admission was fifteen and one half weeks and from onset of symptoms to death sixteen and one half weeks. Local metastases were present in nine of the ten cases, and metastases were widely disseminated in three of the six cases examined post mortem. The outcome was uniformly fatal. In Phillips's series metastases had already involved the lymph nodes in two thirds of the cases and other metastases were found in an unusual variety of sites. The authors emphasize the short course, the extensive metastases and the hopeless prognosis and point out that the condition, while uncommon, is not as rare as is usually thought and therefore the ruling out of gastric cancer because of the youth of a patient suffering from an anomalous type of dyspepsia must be avoided. In such cases the routine use of the flexible gastroscope may aid a diagnosis to be made sufficiently early so that radical but probably beneficial surgery may be carried out.

Glasgow Medical Journal

16:63-114 (Sept.) 1940

Carcinoma of Bronchus: Investigation into Incidence and Pathologic Features of 131 Cases from Glasgow Royal Infirmary. J. C. Dick.—p. 63.

Indian Medical Gazette, Calcutta

75:449-512 (Aug.) 1940

Subtotal Gastrectomy with Uleer Exclusion in Treatment of Chronic Peptic Ulcer. F. A. B. Sheppard.—p. 449.
Report of Pneumonia Enquiry at the Mayo Hospital, Lahore, During the Years 1938, 1939 and 1940. G. F. Taylor and N. L. Chitkara.—p. 456.
New Method for Relief of Paralysis of Opponents Pollicis. M. Scheck.—p. 464.
Automatic Flyproof Latrine Seat. B. S. Dhondy.—p. 466.
Intradermal Test as Index of Vitamin C Nutrition: Part II. S. Banerjee, B. C. Baha and K. C. Basak.—p. 468.
Observations on Outbreak of Epidemic Cerebrospinal Meningitis in Burma, with Special Note on Its Bacteriology and on Progress of the Epidemic. G. C. Maitra and P. N. Sen Gupta.—p. 473.

Lancet, London

2:381-410 (Sept. 28) 1940

*Chronic Jejuno-Ileal Insufficiency: Pathogenesis of Celiac Disease, Tropical Sprue and Other Conditions. T. I. Bennett and C. Harwick.—p. 381.
Potassium and Phosphate Content of Plasma from Stored Blood. B. R. S. Mainwaring, F. X. Aylward and J. F. Wilkinson.—p. 385.
Local Inunction of Testosterone in Chronic Mastitis. A. W. Spence.—p. 387.
Visceral Pain Produced by Balloon Distention of Jejunum. F. H. Bentley and R. H. Smithwick.—p. 389.
Antiseptic Analgesic Tannic Acid Jelly for Burns. J. F. Heggie and R. M. Heggie.—p. 391.

Chronic Jejuno-Ileal Insufficiency.—Bennett and Harwick direct attention to the fact that the last twenty years have seen the increasing recognition of a clinical syndrome of steatorrhea, tetany and macrocytic anemia. The names of Gee, Herter, Heubner and Thaysen have been attached to it; celiac disease and tropical sprue fall within its definition. There is a tendency to class together as nontropical sprue all such cases not coming from the tropics. The syndrome is also found in some cases of malignant or of cicatrizing disease of the small intestine, in some cases of gastrocolic fistula and in some cases of tabes mesenterica. Rickets and deformed bones are common when the syndrome affects children. The anemia is hypochromic or erythroblastic; stomatitis and sore tongue are common; skin lesions, including some resembling those of pellagra, have been described. The fatty diarrhea is notable in that the fat is fully split, and the stools may be bulky and pale but not frequent. In other cases the stools are frequent and gassy; megacolon, perhaps compensatory, is pronounced in some cases. When the syndrome begins in childhood there is stunting of growth, often accompanied by infantilism. When it begins during adult life it is usually accompanied by sterility. Blood calcium and blood phosphorus are often low. In spite of the attempts to recognize in this syndrome a single entity, it seems clear that two diseases in no way related to each other, celiac disease and tropical sprue, are responsible for the vast majority of examples. The following points are important in differentiating between these two conditions: Celiac disease essentially affects little children. Tropical sprue is essentially a disease of adult life. Celiac disease produces meteorism, but in its later stages the stools tend to be pale and bulky rather than frequent; stomatitis and sore tongue are rare; megacolon is common in the older patients. In sprue the feces tend to be more fluid, and the diarrhea responds more rapidly and completely to treatment. Sore tongue and stomatitis are the rule; megacolon seldom if ever develops. Tetany is common in both conditions, but rickets and deformed bones are found in celiac disease alone. The anemia of celiac disease is usually hypochromic. In tropical sprue, macrocytic anemia is common. Established celiac disease is fatal to 40 per cent of the patients during the first two years, and of those who survive the early stages not more than 25 per cent reach the third decade. Tropical sprue, properly treated, gives an extremely good prognosis. Even in the present incomplete state of knowledge it is important to recognize that in every example of this syndrome the clinical picture is due to the same cause; that is, chronic jejuno-ileal insufficiency, with consequent defects of secretion and absorption. The final proof of this is provided by cases in which the small intestine is deprived of its functions by surgical short-circuiting.

Medical Journal of Australia, Sydney

2:229-252 (Sept. 14) 1940

Investigation into Incidence of Pulmonary Tuberculosis in Young Women of Adelaide in the Age Group 15 to 30 Years. H. W. Wunderly.—p. 229.
Study of Tuberculous Cavity of Lung. R. Le P. Muecke.—p. 232.
Tuberculosis as a Problem for the State. C. Harvey.—p. 239.

Tubercle, London

21:281-312 (June) 1940

Topography of Relative Distribution of Cancer and Tuberculosis. D. H. Cruickshank.—p. 281.
Developmental Cystic Lung in an Infant: Case. F. G. Chandler, S. R. Glyne and D. V. Hulme.—p. 292.

Schweizerische medizinische Wochenschrift, Basel

70:801-824 (Aug. 24) 1940

- Transition Forms of Blood Groups. L. Hirsfeld and Amzel.—p. 801.
 *Treatment of Epidemic Poliomyelitis with Potassium Chlorate. O. Gsell.—p. 803.
 Clinical Observations in Case of Beriberi in Switzerland. C. Maier.—p. 807.
 Cystic Dilatation of Ostium in Case of Blind Proximal End of Ureter and in Case of Severe Hypoplasia of Homolateral Kidney. J. Wyler.—p. 809.
 Acute Glaucomatous Cataract Designated as Glaucoma Spots. E. Sommer.—p. 813.
 Arteriosclerosis and Alimentation. J. A. Collazo.—p. 816.
 Use of Mercurial Derivatives for Wounds. E. J. Donzallaz.—p. 816.
 Head Injuries During War. T. Naegeli.—p. 817.

Treatment of Epidemic Poliomyelitis with Potassium Chlorate.—Gsell calls attention to the administration of fractionated doses of potassium chlorate in the treatment of poliomyelitis, a method recommended by Contat (*Schweiz. med. Wchschr.* 68:669 [June 4] 1938; abst. THE JOURNAL July 23, 1938, p. 363). An epidemic of poliomyelitis during 1939, in the course of which 119 cases were observed at Gsell's clinic, gave him an opportunity to ascertain the efficacy of Contat's therapy. Gsell employed potassium chlorate in ninety-seven cases. He presents a number of clinical histories which provide answers to the essential questions that arise in connection with every form of treatment recommended for poliomyelitis. He observed that potassium chlorate exerts no influence on the severest form of poliomyelitis with ascending paralysis. The temperature remains high, the paralysis advances and death takes place. The question whether early potassium chlorate therapy is capable of arresting the process in the preparalytic stage and thus prevent paralysis is likewise answered in the negative. Early potassium chlorate treatment failed to prevent the development of serous meningitis in nonparalytic cases. The fever remained high in spite of the administration of potassium chlorate. Comparing the cases treated with potassium chlorate with cases observed in previous epidemics in which Contat's method was not employed, the author found that the percentage of nonparalytic forms was practically the same. The mortality rate was 6 per cent in the cases treated with potassium chlorate and 1.5 per cent in the other cases. The percentages of complete cure and of crippling defects were about the same whether potassium chlorate was given or not. The author thinks that the higher mortality rate in the cases treated with potassium chlorate is not the result of the treatment but that it indicates that this therapy has no effect on the course of poliomyelitis.

Archivio per le Scienze Mediche, Turin

69:489-576 (June) 1940. Partial Index

- *Regulation of Hemopoiesis in Pathogenesis of Pernicious Anemia: Action of Liver Extract on Basal Metabolism in Pernicious Anemia. G. Boccuzzi and W. Paolino.—p. 489.
 Aminopyrine and Diuresis. C. Franzolin.—p. 511.

Pernicious Anemia.—Boccuzzi and Paolino studied the behavior of basal metabolism in twenty cases of pernicious anemia. The basal metabolism was increased in thirteen and diminished in one case before the employment of liver therapy. It displayed a tendency to become normal after ten or more days of liver therapy. Nine patients were given an intragluteal injection of 4 cc. of liver extract before liver therapy and again in the course of treatment. The consumption of oxygen for the first four hours following the injection progressively increased when the basal metabolism was normal, diminished and then increased when there was basal hypermetabolism and varied slightly in the presence of hypometabolism. Because of the influence of liver extract on pernicious anemia and the frequency of basal metabolic disorders on the one hand and the relationship between the thyroid, hemopoiesis and basal metabolism on the other, the author associated thyroid disorders with the pathogenesis of pernicious anemia. He presupposes the existence of two hemopoietic antipernicious factors, Castle's factor and a hepatothyroid factor. Both factors are stored in the liver and are essential to normal hemopoiesis. The insufficiency of both factors, or the insufficiency of one in the absence of the other, is the cause of a disturbance in the regulation of hemopoiesis

with consequent pernicious anemia. A predominant insufficiency or absence of the Castle factor stimulates overproduction of the hepatothyroid factor with a partial or total reaction on the part of the thyroid. If the reaction is partial, the basal metabolism is normal in the presence of pernicious anemia. If it is total, there is basal hypermetabolism. A predominant insufficiency of the hepatothyroid factor indicates functional or structural insufficiency of the thyroid associated with basal hypometabolism. The tendency of the basal metabolism to return to normal on liver therapy suggests utilization of the antipernicious factors contained in the liver extract and the reestablishment of the hemopoietic function of the organic antipernicious factors. The Castle factor is not related to the consumption of oxygen by the body immediately on administration of liver. The hepatothyroid factor exerts an indirect effect on the consumption of oxygen through the thyroid. The different curves of oxygen consumption immediately after an injection of liver extract indicate a more or less rapid utilization of the antipernicious factors by the body. A constantly increasing curve of oxygen consumption in the presence of normal basal metabolism indicates a moderate insufficiency of the Castle factor, a partial thyroid reaction and immediate utilization of both antipernicious factors. An early downward curve of oxygen consumption followed by a late upward curve in the presence of basal hypermetabolism indicates acute predominant insufficiency of the Castle factor, a total thyroid reaction, early utilization of the Castle factor and late action of the hepatothyroid factor. A slow progressive upward curve of oxygen consumption in the presence of basal hypometabolism indicates a moderate insufficiency of the hepatothyroid factor from functional thyroid insufficiency and an immediate, although slow, organic utilization of the hepatothyroid factor. Slight variations in the curve of oxygen consumption in the presence of basal hypometabolism indicate insufficiency of the hepatothyroid factor due to structural insufficiency of the thyroid.

Athena, Rome

9:225-256 (Aug.) 1940. Partial Index

- Sulfanilamide in Therapy of Infections of the Eyes. D. Cattaneo.—p. 231.
 *Toxicity of Sulfanilamide for Liver. G. De Bonis.—p. 248.

Toxicity of Sulfanilamide for Liver.—De Bonis observed symptoms of liver intoxication develop in the course of the first week of sulfanilamide therapy in two cases. Gonorrhea in one case and diplococcic tonsillitis in the other were mild and were in a stage of regression when the treatment was instituted. The patients had never complained of liver disorder. The daily dose of the drug was 1.8 Gm. The patients complained three or four days after the beginning of the treatment of nausea, digestive disturbances, headache and a dull pain in the region of the liver. These symptoms were followed from two to three days later by jaundice, urobilinuria and enlargement of the liver. The blood was normal. The drug was discontinued and a proper diet and treatment instituted. The symptoms, however, became more acute, fever developed, lasted one day, abated after spontaneous sudation and was followed by urticaria in one case and by a cutaneous rash in the other. The condition was controlled in two weeks by diet and by appropriate treatment, intravenous dextrose, calcium and liver therapy. The author studied the effect of sulfanilamide on the liver in eleven normal persons who received a daily dose of 0.03 Gm. for each kilogram of body weight for ten consecutive days. Liver function before and after administration of sulfanilamide was determined by the aminoacetic acid and dextrose tolerance tests. Disturbance of liver function was demonstrated in five cases. The author concludes that sulfanilamide has a toxic effect on the liver in a large percentage of cases. It is therefore suggested that particular attention be paid to hygiene and diet before and during administration of the treatment, the dose and duration of which are to be directed by the physician. It is likewise advisable to watch liver function in the course of the treatment, especially in cases in which there is a previous history of liver disorder.

Minerva Medica, Turin

1:545-576 (June 30) 1940. Partial Index

*Strophanthus in Heart Disease. S. G. Jucker.—p. 545.
Roentgenograms of Venereal Lymphogranulomatosis in Anus, Rectum and Colon. M. Buisson and A. Midana.—p. 550.

Strophanthus in Heart Disease.—Jucker administered strophanthus intravenously in seventy-five cases of decompensated heart of various types, such as those due to valvular disease from rheumatic endocarditis, to myocardial sclerosis or to syphilitic chronic aortitis with an anginal syndrome and to failing of the pulmonary circulation due to sclerosis of the pulmonary artery and acute insufficiency of the heart. The treatment was resorted to after failure of digitalis or in cases of intolerance to digitalis. The initial dose amounted to 0.0001 or 0.0002 Gm. of the drug. The total daily dose did not exceed 0.00025 Gm. in disturbances of the coronary circulation, acute heart insufficiency or grave myocardial alterations complicating infections, and it was 0.0005 Gm. in cases without these disturbances and with hypertrophied heart. The drug was administered every other day or at longer intervals, and the total number of doses varied from four to ten. The treatment was repeated in some cases on reappearance of the symptoms of decompensation three or more months after the first treatment. It was well tolerated in all cases. Circulation and the general condition of the patients improved. Oxygenation of venous blood in valvular disease or of arterial blood in sclerosis of the pulmonary artery improved. Diuresis increased and edema was controlled. Dyspnea and cyanosis were controlled or greatly improved. The anginal syndrome in chronic syphilitic aortitis was controlled. The electrocardiogram became normal in cases of valvular disease. It improved in some cases of myocardial disease and did not change in syphilitic aortitis. The treatment is harmless, provided it is given in a proper dose and according to proper indications. Certain types of heart insufficiency are associated with cardiac hypersensitivity to strophanthus. The individual sensitivity is determined by the reaction of the patient to small doses of 0.0001 or 0.0002 Gm. of the drug. The author considers acute insufficiency of the heart as an absolute indication for strophanthus therapy. The presence of moderate renal disease or of complicating myocardial sclerosis does not contraindicate the treatment. Addition of dextrose, caffeine or ethylenediamine does not modify the pharmacologic properties of the drug.

Boletín de la Asociación Médica de Puerto Rico

32:313-352 (Sept.) 1940. Partial Index

Adenoma of Kidney: Case. P. G. Curbelo.—p. 313.

*Nutritional Edema. A. Ortiz.—p. 319.

Nutritional Edema.—Ortiz emphasizes the role of lack of proteins and vitamins A and B₂ in the diet in the development of nutritional edema frequently seen in Puerto Rican infants and children. Twenty-seven children with nutritional edema observed by the author were anemic and undernourished and they complained of general debility. Five patients in the group vomited, twenty-five had chronic diarrhea, and several suffered from pellagra, celiac disease, intestinal parasites, infectious fever, chronic bronchitis and multiple infections. One had pulmonary tuberculosis. The treatment consisted of a diet rich in proteins and of administration of vitamins A and B₂ and, in grave cases, of liver extract, iron and blood transfusion. The proteins in the blood plasma were determined before and after the treatment in nine cases, in all of which, except those complicated by renal disease, the total proteins and albumins in the blood were increased coincidentally with the control of edema by diet and treatment. In cases of nephritis or nephrosis the treatment controlled edema but the blood proteins did not increase. A differential diagnosis between nutritional edema and renal disease is important because restriction of proteins, which is indicated in the latter, aggravates the former. Patients with early nutritional edema react promptly and favorably to the treatment and diet. The diet must be supervised when the patient returns to his home because of poverty and lack of understanding of the causes of the condition. The lack of a proper diet results in reestablishment of edema. Two necropsies revealed anatomopathologic evidence of lack of vitamin A and of the occurrence of multiple infection.

Revista Medica de Rosario, Rosario de Santa Fe

30:807-900 (Aug.) 1940. Partial Index

Femininity Causing Effects of Adrenal Tumors in Men. O. Pico Estrada.—p. 807.

*Relationship Between Chronic Mastitis and Cancer of Female Breast. S. Warren.—p. 829.

Chronic Mastitis and Cancer of Female Breast.—Warren studied 1,044 women who had chronic mastitis and in whom a portion of the involved breast was removed and was subjected to microscopic study. The group included cases of chronic simple and cystic mastitis, Schimmelbusch's disease, Semb's cystic fibro-adenomatosis, Cheate and Cutler's hyperplasia, Aschoff's cystic mastopathy and Reclus's disease. The patients were observed for an average period of nine years after the operation. Cancer of the involved breast did not exist in any case at the time the operation was performed. It developed in thirty-five cases some time after the operation. The author found that the incidence of cancer of the breast was six times as great in women who have had chronic simple or cystic mastitis as in those who did not have this condition. It was greater in women above the age of 30 and before the menopause than in those at the menopause or after. There exists a relationship between chronic mastitis and the development of cancer, although either condition may develop in the absence of the other. The treatment of chronic simple or cystic mastitis consists in excision of the involved portion of the breast. The patients should be observed for a long period after the operation. The appearance of nodules or cysts in the remaining portion of the breast is an indication for a unilateral mastectomy. A bilateral mastectomy is not justified as a preventive measure in cases of chronic simple or cystic mastitis.

Zeitschrift für Urologie, Leipzig

34:129-192 (No. 4) 1940. Partial Index

*Prostatectomy or Resection of Prostate? O. Kneise.—p. 129.

Abrodil Pool According to Kneise-Schober and Its Significance for Diagnosis of Hypertrophy of Prostate. K. L. Schober.—p. 139.

*Technic and Interpretation of Acid-Alkali Alteration Test According to E. Rehn. H. Schneider.—p. 148.

*Failure of Indigo Carmine Test and Significance of Acid-Alkali Alteration Test According to E. Rehn for Diagnosis of Renal Tuberculosis. Annemarie Schneider.—p. 157.

Renal Injuries. P. Deuticke.—p. 165.

Cleansing, Sterilization, Drying, Hardening and Storage of Urethral Catheters. W. Wicher.—p. 173.

Prostatectomy or Resection of Prostate?—Kneise cites a number of recent publications on the question of enucleation versus electroresection of prostatic hypertrophy. He considers the enthusiasm for the transurethral electrocoagulation and electrotomy as premature. In an earlier evaluation he had expressed the opinion that electrocoagulation is excellent for the soft tumors but that in hypertrophy of the prostate the method will not produce such wonderful results, for, he is convinced, the extremely favorable results reported by some are due to the fact that electrotomy was employed in cases which would have responded to catheterization. He cites authors who greatly restrict the indications for electroresection and quotes statistics from Rehn's clinic in Freiburg which reveal that the percentage of patients subjected to electrocoagulation has steadily declined in recent years. On the basis of thirty years of experience he himself favors a two stage prostatectomy. With this method he has been able to save patients who at first seemed unsuited for the operation. However, some times he has waited as long as six or nine months to give the kidneys time to recover sufficiently, so that the intervention could be made without danger. He admits that prominent surgeons state that from 25 to 30 per cent of their patients cannot be rendered suitable for operation and that for these they wish to employ electroresection, but he thinks that this is due to the fact that they do not evaluate properly the temporary vesical fistula. He stresses the advantages of the vesical fistula and describes his method of effecting the gradual closure of such a fistula. He believes Kraas justified in stating that it is not advisable to treat all forms of prostatic adenoma with the same method, and that the possibility of individualizing the treatment signifies progress of prostatic surgery. Large adenomas of the prostate should be radically removed by prostatectomy, provided the case is suitable for operation.

Rehn's Acid-Alkali Alteration Test.—According to Schneider the acid-alkali alteration test was first described by Rehn and Günzburg in 1923. Since then it has been employed in about 4,000 cases at the surgical clinic in Freiburg. Rehn's acid-alkali alteration test examines the capacity of the kidney to eliminate acid and alkali and to reabsorb the necessary alkali. The acid elimination is tested in the morning with the patient fasting. One hour before the examination the patient is given 300 cc. of water and twenty-five drops of diluted hydrochloric acid. A rack with two sets of test tubes (one set for the urine from each kidney) is prepared. Cystoscopy is done and ureteral catheters are introduced. The pH value is determined with five drops of urine from each kidney. Then follows the alkali tolerance test, 50 cc. of a 4 per cent solution of sodium bicarbonate being injected intravenously. Three minutes later and at intervals of three minutes (until twelve minutes has elapsed), urine is obtained from both kidneys and the pH of the specimens is determined. It is absolutely necessary that only those specimens be compared which were excreted simultaneously by the two kidneys. The kidneys of a healthy subject excrete at the same time urine of an identical reaction, but even slight differences are pathologic. Thus in the evaluation of the curve obtained by the acid-alkali alteration test the absolute pH values are less important than the functional latitude (the change after the alkali tolerance test) and especially the comparative values of the two kidneys. The author believes that the determination of the pH values is the chief reason why the method has failed to obtain the wide application it deserves. Rehn's modification of the indicator method of Michaelis is the best for practical purposes. In case of extensive glomerular impairment the acid-alkali alteration test discloses a persistent acidity (acid rigidity). The impaired glomeruli are throttled. The flooding of the blood with an alkali produces no change, because a better elimination is impossible. The urine remains acid. In case of slight glomerular damage the acid rigidity is relative; the curve of the diseased kidney remains below that of the healthy one. In case of tubular lesions, although the glomeruli eliminate the acid and alkali the diseased tubules fail to reabsorb alkali and already the initial value of the diseased kidney is at the neutral point or in the alkaline sphere, and after the alkali tolerance test the alkali values become extremely high. If glomeruli and tubules are impaired, the reaction of the renal urine is from the beginning near the neutral point or in the alkaline region. The acid-alkali test is extremely sensitive. It has proved especially valuable in the diagnosis of renal tuberculosis, disclosing disorders not detectable by other tests.

Acid-Alkali Alteration Test in Renal Tuberculosis.—The diagnosis of renal tuberculosis is generally based on the presence of renal pyuria, disordered renal function and tubercle bacilli in the renal urine. Tubercle bacilli cannot always be demonstrated in the presence of renal tuberculosis. In such cases the diagnosis is made on the basis of functional kidney tests combined with evidence of destruction in retrograde pyelograms. At Rehn's clinic, according to Schneider, the diagnosis is never based on the pyelogram alone or on the functional tests alone, for neither alone permits of a reliable diagnosis. If both are positive, renal tuberculosis can be recognized even if no bacilli can be demonstrated. Extreme caution is necessary in the interpretation of roentgenograms, because there exist non-tuberculous inflammatory lesions in which the changes in the papillae may resemble those of an incipient renal tuberculosis. Differentiation is possible because renal tuberculosis is always accompanied by permanent disturbances in the renal function, whereas the nontuberculous papillitis may heal and the function may become normal. Since functional tests are of decisive importance in the diagnosis of renal tuberculosis, their reliability was investigated and it was found that the indigo carmine test often simulates a normal function when the acid-alkali alteration test of Rehn discloses a functional impairment. The more reliable acid-alkaline alteration test has not found the wide application it deserves, because the impression prevails that it is too complicated. The author feels that this impression is not justified. She presents a number of case histories which demonstrate that Rehn's acid-alkali alteration test is definitely superior to the indigo carmine test, for whereas the indigo carmine test simulated a normal renal function, the acid-alkali alteration test disclosed a functional disturbance of the diseased kidney.

Nordisk Medicin, Gothenburg

7:1269-1302 (July 27) 1940

Hospitalstidende

*Bone Destruction in Cancer of Cervix of Uterus by Direct Propagation, by Lymphogenic and by Hematogenic Metastasis. F. Nørgaard.—p. 1271.

Bone Destruction in Cancer of Cervix.—Nørgaard says that x-ray examination of the skeletal system, especially of the lumbar spine and the pelvis, in patients with cancer of the neck of the uterus treated at the Radium Station in Copenhagen shows that the changes consist almost exclusively in osseous destruction, in a few cases with sclerosis. Since propagation or recurrence of the cancer almost always occurs in only two ways, either to the parametrium or to the lymph glands along the vasa iliaca and the abdominal aorta, there are two well defined main groups of osseous changes. When there is metastasis to the parametrium the earliest changes appear in the iliopectineal line and consist of a flat irregular gnawing off a few centimeters in extent, usually localized to the posterior half, occasionally with sclerosis. In more advanced cases the iliopectineal line is frayed or gnawed off, with larger or smaller clarifications, often sharply defined, from the sacro-iliac articulation to the pectineal line and upward on the inner side of the ala of the ilium. Every small clarification in the iliopectineal line must be suspected as possibly the earliest faint sign of destruction. In the second main group, with metastasis to the regional lymph glands, the tumor tissue may invade the adjacent bones; in the ala of the sacrum and parts of the ilium bordering on the sacro-iliac articulation clarifications appear, and in the lumbar vertebrae, most often the fourth and third, destruction occurs in the lateral surfaces of the bodies, usually unilaterally. There may be extensive destruction in several vertebrae. Hematogenic metastases to bone are rare. The author has seen five cases in fourteen years, two of which were localized to the femur, two to the tibia and one to the tarsus. In one of the cases roentgen irradiation resulted in recovery; the patient has been without symptoms for over four years. He cautions that the osseous changes described must not be confused with changes in the neck of the femur resulting from roentgen irradiation and causing spontaneous fractures and pseudarthroses.

Norsk Magasin for Lægevidenskaben

*Traumatic Pulsating Exophthalmos and Its Treatment. E. Schie.—p. 1275.

*Neuro-Anatomic Examination of Brain After Ligation of Carotid Artery in Case of Pulsating Exophthalmos. J. Cammermeyer.—p. 1283.
Fracture of Spinal Column After Metrazol Shock Treatment of Psychoses. A. Vogt.—p. 1289.

Traumatic Pulsating Exophthalmos and Its Treatment.—In the first of Schie's patients, a man aged 36, the symptoms disappeared for a week after ligation of the right internal carotid artery on the same side as the aneurysm. They again disappeared after ligation of the left internal carotid and the patient felt well for four days. An apoplectiform hemiplegia of the right side then occurred, with fatal outcome. In the second patient, a woman aged 41, ligation of the internal carotid on the same side as the aneurysm was done. While normal eyesight was not restored, the other symptoms disappeared and she is able to work. The third case is one of untreated pulsating exophthalmos of six years' standing.

Neuro-Anatomic Examination of Brain after Ligation of Carotid Artery.—Cammermeyer's examination in the first of Schie's cases of pulsating exophthalmos showed a considerable degenerative process in the left hemisphere, limited to the cortex within the motor area and the adjacent convolutions. The cellular changes were of the "severe" (Nissl) and the "homogenized" (Spielmeyer) types. The glia cells in part showed regressive changes with pyknosis and karyorrhexis, in part milder "progressive nuclear changes." The author concludes that following the ligation of the carotid on the left side a considerable necrosis of the cortex, ascribed to a probable embolic process, occurred corresponding to the end branchings of the middle cerebral artery. In the intensity and nature of the changes and their limitations the case resembles the cases examined by Müller and Döring, but it differs from them in that the pathologic changes are cortical without involvement of the white substance or the basal ganglions. The onset of symptoms an interval after the operation also suggests an embolic pathogenesis.

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DaCosta—Man and Genius

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PHILADELPHIA

Every so often a truly great soul or character is born, one who is extraordinary and grand and whose mental ability shines out with the seeming brilliance of the noonday sun, rendering all around refulgent with its scintillating rays. Occasional fleeting shadows may dim the rays and give a hasty glimpse of those characteristics, showing that genius is just human and that such a giant is, after all, akin to us poor ordinary mortals. Occasionally too one may be privileged to tread the pathway carved by such a genius or at times walk beside him and see and attempt to analyze some of those characteristics.

For only a short time was I privileged to stand near such a genius and to observe him for a few fleeting moments, but those fleeting moments have made a lasting impression—a bright ray—a beacon outshining the light of other knowledge that has come to me. I refer to that genius of pen and scalpel, that master of oratory, that omnivorous reader, that great philosopher, that almost matchless mind and yet very human J. Chalmers DaCosta. A definite and unswerving teacher who hated an ice bag in appendicitis with the same vehemence that he hated lawyers who browbeat the physician on the witness stand, to whom a fire or a fireman meant more than a fat fee and to whom the gratitude of a ward patient meant a greater personal satisfaction and recompense than the dollars of the wealthy. A man whose force of knowledge, will power and deft fingers stalked, time and time again, the grim specter and won on that twin field of tragedy and pathology called the operating room.

His book on surgery, true to his teachings, was and still is a revelation and a masterpiece. The usual dry preface was replaced by an entertaining essay, varied in each edition and showing the diversified knowledge of the author in arts and sciences as well as an understanding of what would appeal to all classes of readers.

TRIALS AND TRIUMPHS OF THE SURGEON

Stories always crop up about such an individual—some true, some spurious—but each serves to emphasize the personal element. They

never detract; they serve to delineate and cause him to stand out in bold relief both among his contemporaries and in the times and greatly accentuate the God-given genius in his mortal habitation. No better illustration can be used in the opening pages of this character sketch than some of the remarkable figures of speech, comparisons and descriptions used in one of his speeches, notably *Trials and Triumphs of the Surgeon*: "When a surgeon is too old to be of much value they make him a consultant, but when a lawyer is ready for the shelf he is placed in the Supreme Court. When I see his honor, the judge, on the bench, with his arcus senilis, tortuous temporal arteries and other signs of degeneration, I think of the fly in the amber; I see him, I know he is there, but how did he ever get there?" To quote further: "It is vastly to the credit of the medical profession that so few leave it to go into quackery; . . . if a regular chooses to apostasize and then turn quack he can often make money rapidly and in quantity, but few are willing to become pariahs. The old training has left its mark. Certain beliefs are fixed so firmly that they become as intuitions. A man may leave the army of healing but he seldom joins the enemy. . . . Failure, disappointment, disenchantment, embitterment, neglect, even actual want very seldom cause a physician to become a quack and thus cease to be a man who stands above the common herd." "Of all the causes of failure I doubt if any is more potent than vanity. The proper attitude towards all scientific questions is one of humility. When one can no longer wonder at nature, he can no longer progress. When he would settle everything by a formula, he is consigned forever to the compartment of useless odds and ends." "Vanity tires out even the most patient colleague, gives a weapon to every opponent, and potential friends quickly weary of the society of the discoverer of everything that is useful and important. Such men obey the command to let their light shine before men, and it shines so strongly and persistently that it resembles a conflagration in a shop of fireworks.

It may be added that those about find their nostrils assailed with noisome odors and their ears bombarded with sounds of destruction. Were the walls which bar the way to success like the walls of Jericho, they might be expected to fall from noise, but they do not do so. The man who does the bombarding is of small caliber in spite of being a big bore. Every now and then we see such a man purchase a two-cent stamp as though he were laying the cornerstone of a cathedral. Such a vanity makes one suspicious, critical, resentful, ungrateful and bombastic. The athletic exercise of throwing bouquets at oneself never strengthens the muscles of the mind. When it is practiced for a long time, a man sets as exaggerated an estimate on his own value as though he were suing a railroad company for damages. Such a man can't obtain real success, but he may get rich, because he may persuade the general public to take him at his own estimate."

"The vain man in surgery is a deadly peril. He mistakes his own half-formed opinions for the oracles speaking within him. He is never conscious of his mistakes and hence keeps on making them. He misleads others by his positive assertions regarding unproved views. He clamors insistently for credit. What he aims at is to attract attention. He would rather be abused than not spoken about at all. He has noticed the fact that a plain, modest, hard-working man, doing his duty and serving humanity, attracts no more real attention than a thermometer on a balmy day. It is a sad commentary on the world that bow legs attract more attention than great virtues, and that a red nose causes more comment than a blameless life."

"A surgeon is like a postage stamp. He is useless when stuck on himself. A vain surgeon is like a milking stool; of no use except when sat upon. I don't see how any real surgeon can be vain. He is too often near to the inscrutable mystery of death—he sees too often the weaknesses of men—he too often stands at cross roads of judgment, knows that one way is the wrong way, but finds no sign to mark it—he too often has to reproach himself for mistakes—he too often sees calamity tread on the heels of calamity—he too often laments, impotent to save and watches 'Beauty and anguish walking hand and hand, the downward way to death'—he knows too well that Sophocles spoke the truth when he said:

The power of learning may a while prevail,
A time prolong a mortal's fleeting breath,
But useless all her arts are to avail
To conquer Fate or check the hand of Death.

"I don't see how any surgeon can be vain any more than I can see how an astronomer could be vain—an astronomer who peers into

the depths of infinite space which the hand of Omnipotence has strewn thick with star dust."

"Real success comes only from persistent hard work. No lily handed child of ease is entitled to it or can have it. Its insignia do not come from the general public but are conferred by the profession itself. Any temperament which keeps a man from sticking at it forbids success. Mere episodes of busy idleness do not constitute work. The loafer is a failure. To loaf in front of a church is just the same as to loaf in front of a saloon. One may loaf in a library, a laboratory, a hospital, as well as on a street corner, in a bar room, or at an afternoon tea. Indolence sterilizes the mind, but work will not create genius. It is an infinitely rare gift to dream the fairy tales of science. Genius alone dreams them, but even genius must work to make them real. I believe that real success can come only from work, but I know that even the hardest work may not command it. 'Tis not in mortals to command success.' Some work wrong and fail. Some work right and fail. Some work but fail 'until they grasp the skirt of happy chance,' by which they are dragged to the openings they lacked and the opportunities they despaired of obtaining. No man could dive for pearls on a mountain; no man could become an astronomer in a cave, and it may be impossible to create opportunity."

ACCEPTANCE OF RESPONSIBILITY

Only an analytical, understanding, philosophical, God-fearing mind could give voice to such reasoning. Only a man whose mind and heart strings, duty and cares have been rendered responsive to burden and responsibility could have laid bare his soul as follows:

"A surgeon's life is a hard one. It is a life of endless strain. During most of the hours of every day his faculties are keyed up tense almost to the breaking point, and physical tire goes hand in hand with mental exhaustion. He must carry and carry naturally the heaviest responsibilities. No matter how tired he is, his faculties must be alert, his judgment clear, his will inflexible, his knowledge accurate and instantaneously accessible for transmission into action. He must be calm, no matter what the clamor, the peril, the perplexity. Of course he will worry about his patients. Every conscientious man must do so. A man who doesn't worry at all doesn't care a whole lot. I should not want a man who did not care a whole lot operating upon me or mine. Perhaps worry is a device of nature to make us try to do our very best. If we knew we should not worry, we might be tempted at times to be careless. If a surgeon analyzes his worry he can get a line on what sort of man he is himself. If he worries only because he fears he may be sued, may lose

a bill or may hurt his reputation, then with him the voice of conscience is the fear of getting caught. If he worries because of the poor patient and the credit of surgery, then he is really a conscientious man. He must expect much harsh and unjust criticism and when he is the victim of it all he can do is follow Joseph Pancoast's advice and make his shoulders broad enough to bear the burden. A surgeon must learn thorough self surrender and all his life must wear the iron yoke of duty."

"Yes! the life of a surgeon is toilsome, responsible and anxious. It is a life of stress and strain. It is small wonder that surgeons as a class are not long lived. Pneumonia, angina pectoris, Bright's disease, vascular disease are the commonest agents of dissolution. The life is full of tragedy. Sometimes it seems as though a malign destiny were intervening in our affairs."

"The days of waiting for practice are very hard and very dangerous. Those days may make a man or mar him. The same wind which blows out the penny dip urges the flames of the forest fire. Those days go far in determining what sort of a man he is and is to be. During them he should study ceaselessly, learn to work, to observe, to think, and to teach himself. He should ponder deeply and often on the responsibilities and the duties of his calling. Thus he should become a real man, an individual, a man with genuine ideas, definite beliefs, established principles and high ideals. Thus he should avoid being a mere mimic and echo."

"There is grave danger in those waiting hours, those dark hours of poverty and nonrecognition. A sensitive soul will shrink, falter and probably fail. Brooding discontent is apt to dominate, and it is a deadly peril. Jealousy may spring up, envy may attain rank luxuriance, bitterness may grow, selfishness, avarice, disloyalty, mental dishonesty may be planted. Low ideals are ever knocking for admission. From them come admiration for despicable things, desires for unworthy objects and improper professional conduct."

The frequency with which he repeats himself is striking, but the explanation is freely given in a footnote in the Papers and Speeches of DaCosta: "I quote myself at times. Such quotations may mean scantiness of mental resources, but may also be due to profound conviction. If one believes he must preach and repeat. The great Carlyle did so often, surely an insect may."

His tribute to man's research and the enormous number of things yet to be discovered are shown in his frequent repeated expression "The first few hesitating words of truth have, as yet, but scarce been lisped by the baby lips of Science," as well as his profound reverence is illustrated and thoroughly impressed on his

own mind, for he repeatedly speaks of "the depths of infinite space which the hand of Omnipotence has strewn thick with star dust."

No greater tribute could have been paid to a man than was given to DaCosta by Francis T. Stewart before a class in the surgical amphitheater in Jefferson Medical College of Philadelphia in 1917 when, in describing a rare and unusual case, he said "I wished to know something about this condition, I asked Professor DaCosta, and as was always the case, I received concise information—he told me who first described the condition and when; who and where the first operation was performed; the present status of the operation with the improvements."

A RETENTIVE MEMORY

During his last illness in the hospital a doctor in visiting him spoke of Dickens, and DaCosta quoted at length from *Dombey and Son*. The doctor went home and looked up the quotation in the book. As near as he could tell the quotation had consumed several pages of the book, word for word. This visitor was not satisfied and made it a point to call on this ill surgeon a few days later and brought up the subject of *Dombey and Son*, asking when he had read it. DaCosta said "I have not had that book in my hands for over twenty-five years."

He was the same with all medical subjects. He knew; he possessed knowledge. It was an inspiration to be in his presence. His lectures were a mastery of diction and information; he never sidestepped a point but was emphatic, concise and dogmatic in his views. One was never in any doubt either of his knowledge, his authority or his position on any matter or subject. As a friend he was superb; as a foe, implacable. Who that ever heard could forget the lecture on appendicitis: "Appendicitis is inflammation of the vermiform appendix; it is characterized by abdominal pain, which is often general, colicky in nature but sooner or later localizes in the right iliac fossa; there is often nausea and vomiting, there may or may not be constipation; there is usually fever and leukocytosis; there is localized tenderness and rigidity, headache may be present, but abdominal pain which has been preceded by headache is not appendicitis."

ATTITUDE TOWARD WOMEN

His "pet peeve" however, seems to have been women. He observes that Dickens's description of Sairey Camp and Betsy Prig portrayed clearly the nurse as she was about seventy-five years ago, "A hideous affront to intelligence and an insult to humanity, often dirty, generally unscrupulous, usually drunk and always ignorant." The same often applied to the early

nurse in The Old Blockley. However, the modern nurse was characterized as the antithesis of the oldtime hireling—well educated, clean, intelligent, refined, conscientious, she is truly the right hand of the physician. DaCosta read all the works of Mary Roberts Rinehart, of whom he was very fond, but in an article entitled *Suicide*, read before the American Philosophical Society, he waxes eloquent regarding women: "Of late there has arisen a disposition to bring women into the forum to combat with men while the home takes care of itself. Those possessed of this disposition repudiate anatomy, spurn physiology, and disregard religion, history and common sense. Woman is not competent in man's work, she is inefficient, she loses at least twice as much time from sickness and she breaks down under sudden strains of overwork or difficulty."

"When she works as a man she must put aside not only many charms and prejudices but womanly things in general, and among those things she must put aside are healthy babies, the home and the rearing of children, and God Almighty constructed her bodily to bear children and mentally to rear them. Such women may have children but the job is usually very ill done. She cannot do properly what she was built to do. . . . If a woman invades man's callings she will pay a dreadful penalty in insanity, suicide, and in the delivery of her progeny; she will wreck the chief hope of the civilization, the clean, decent, happy home. If she works as a man she will be treated as a man and will be subjected as is a man to a multitude of irritations, depressions and worries from which she is now free. A woman's real profession is matrimony and she often makes a bad failure even in her natural profession. To make a success of this will require all her ability and energy, tact and self sacrifice. She had best leave man's affairs to man." "The blatant and militant suffragette is well along on the highway of degeneration."

A man cannot write concerning his chosen profession or teach the subject nearest his heart without weaving his own soul into it. The many editions of DaCosta's *Surgery*, his many scientific articles, his marvelous lectures, the honors and degrees heaped on him are too well known to be repeated or can well be imagined. He often settled arguments in a peculiar though philosophical manner. On one occasion when at a surgical convocation two groups of surgeons were presenting cholecystectomy versus cholecystotomy, and when he was called on to open the discussion, DaCosta's nimble mind offered this. "I have listened to the distinguished surgeons from the East argue for

cholecystotomy; I have listened to the equally distinguished gentlemen from the West argue for cholecystectomy. Gentlemen, it is all a matter of experience, but experience doesn't prove a thing or there would not be such a thing in the world as bigamy."

RADICAL AND CONSERVATIVE SURGEONS

In contrasting the two varieties of surgeons, he wove his ideals, his hates, his hopes, his detestations, his tolerance, his intolerance, his happiness, his sorrows and his knowledge into a glorious landscape of words and phrases, where the dead trees only served to accentuate the glory of the living verdure; where the mountain tops of knowledge were rendered the higher by contrast above the abysmal valleys of ignorance; where the clouds of doubt and dismay modified the soft rosy tints of the daybreak of science and the rising sun of achievement.

"Gradually, as a man becomes a surgeon, he tends toward one of the two fundamental groups into which all surgeons are divisible. The mental tendencies of an individual determine to which group their possessor or victim belongs. Each type has its strengths and its weaknesses. Each may be potent for good or active for evil. The ideal surgeon has not as yet been born. He would possess the strengths of both types and the weaknesses of neither. He would have wisdom as well as knowledge—tact as well as skill—confident hope as well as cautious doubt. His hand, like that of Joseph Pancoast, would be as light as floating perfume—his eye as quick as a flashing sunbeam—his heart as broad as humanity—his soul as sweet as the waters of Lebanon."

"One fundamental class is the conservative, the other is the radical. The conservative is often a most valuable factor in surgery. He is a brake on the wheel and often stops the dashing automobile of progress when on a joy ride from upsetting in the ditch of folly. He smothers the torch of the fantastic, snatches the mask from pretense and punctures the hot air balloon of egotism. He studies the past and reveres it, likes to penetrate its cities and its silences, to repeople its mouldering ruins, and to worship at its shattered shrines, and, in the words of Macaulay, looks back upon some Golden Age that has had no existence outside of his own mind. He attaches an exaggerated importance to books, and minimizes the value of new methods of communicating ideas. He has a great respect for authorities, and would rather 'sin with Pope than shine with Pye.' He is prone to write ponderous treatises, each of which has a name so complicated that it sounds like a sobriety test. He is apt to regard present day claims through the dim sublimation of the foggy and remote. He regards each so-called 'new'

thing as a wrong basely done to the established order and agrees with Solomon that there is no new thing. He is very doubtful of the possibility of reforming anything or anybody. He follows custom even when it is unreasonable or actually absurd. His headlight, like the light of the glow worm, is on the wrong end. He progresses, but in a circle, like the hands of a clock. He is not the active minded man behind the gun, but the slow and often dull man behind the times. His ideas are from a reservoir and not from a spring. Such conservatism may be temperamental opposition to change, may be a mask for incapacity, or an excuse for laziness. He may block or drag back the auto of progress even when it is moving surely, in the right direction and on the right road. He is apt to be a pessimist—seeing the thorns and not the roses—seeing the hole in the doughnut, but not the doughnut.

"The best and most useful conservative is one who has the radicalism of youth and inexperience corrected by age and experience. He is cautious of accepting new things, but can be brought to believe them. He leans to traditional notions, but may be divorced from them after showing him the conduct of the correspondent Error. He will make no successes which will shake the world, but he will make few irremediable blunders. In trying conscientiously to reach a decision, he will often be plunged neck deep in a barrel of quandary. He will be a careful and successful but not a brilliant or notably rapid operator. He will probably be respected, learned, and prosperous."

"A conservative man, when he looks through the spectacles of conservatism, will see common things with the greatest clearness and will come to know them with absolute certainty, but he will be unable to recognize the Good Fairy coming in the loathsome disguise of a Discovery."

"Our most splendid triumphs, our worst mistakes, and our saddest failures come from the radical mind. It is a spring and not a reservoir. It is a voice and not an echo. In the radical group are the original thinkers, the investigators, the discoverers, the combative spirits who 'fight like raging devils for conciliation and hate each other for the love of God.' The real radical believes a new statement because it is new, and doubts an old view because it is old. He blazes the way for lesser minds but is always in danger of being lost in the jungle. His feet may be in the muck heap, but his head is among the stars of space. He is a dreamer of dreams. If he were to lose a leg, he would congratulate himself that he now had but one foot to keep warm. He habitually ignores the reasonably probable and revels in the doubtfully positive. His ideals are broad, expansive, on a great scale. He is ever seeking to make converts. He has

an utter contempt for authority. He jumps to conclusions and may make the champion long distance leap from the frying pan into the fire. He has fierce controversies, devises operations, founds hypotheses, launches theories, discovers diseases, and dazzles all who know him by brilliant flights and amazing activities. As an operator he is brilliant, relying upon skill more than judgment, taking desperate chances, and skimming almost gaily within a hair's breadth of the deadliest catastrophes. He needs to have ever on duty by his side a peculiarly attentive guardian angel. He is never moderate, in fact, he scorns moderation. He is invariably convinced that he is always right. He will not brook contradiction and regards opponents as instigated by the worst possible motives. His knife may cut for good or ill. He obtains wonderful successes and makes dreadful mistakes. He is often a copious and hasty writer, rather prone to recording things as certain long before they are proved. He loudly claims credit he thinks his due. He rides the Rosinante of a hobby as though it were a splendid charger. He often fails to reach his goal and, like a squirrel in a cage, rises only to fall.

"The best type of the radical makes the real progress of humanity. Such a great man is a most attractive personality. He may die poor through adhering to some ideal."

WILLINGNESS TO RECOGNIZE OTHERS

There is another peculiar claim to greatness, rare, but possessed by this man, namely his willingness to pay tribute to ability and accomplishment of others. The baseness of ingratitude shook him deeply, for he said "I am impressed by ingratitude, the ingratitude of patients and in assistants whom I have helped and, believe me, I have experienced both." A veritable anguish is in the heart of one who will say "The death of a patient after an operation is always hard to bear; it is particularly hard to bear if unexpected. Did any one of you ever have a patient die from an anesthetic? I did. It was horrible. Such an event will shake the strongest man."

He accepted the illness which caused his death as the true leader he was, for a man to be a leader must be primarily a soldier, accepting a soldier's life, a soldier's sacrifice, a soldier's glory and a soldier's death. He chose early in life a variable star to follow—the twin star of service and duty. He followed it constantly, consistently, energetically and courageously. He has joined the immortals, but he has immortalized himself in American surgery and in the hearts and minds of all who were fortunate enough to bask in the radiance of his knowledge and glory.

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Teaching Surgery

W. T. COUGHLIN, M.D.
ST. LOUIS

Those of us who are old enough to remember the condition of our hospitals and the character of the surgery practiced in them, even in the first decade of this century, alone are able to appreciate properly the changes that have occurred and the progress that has been made. The surgical profession of this country for the past twenty-five years has continuously and strongly emphasized the idea of improvement of the care of the surgical patient.

The most certain indication of a better and better outlook for surgery is this: The medical schools are going to teach it as a specialty; graduate courses for the study of surgery in medical schools are every year becoming more and more sought after by those qualified, and the number of graduates who have already served as interns and who are willing to spend the additional time and money in order to qualify themselves to meet the requirements of the American Board is gratifying. If the rule that "a man must learn to do by doing" were literally true, then no one could ever learn to practice until after he had practiced. But a man can become qualified to perform surgical operations without "slaying his thousands." He may do that by becoming an assistant to some well qualified surgeon who is also qualified to teach him (such are scarce); or he may enter on a period of special training in medical school and hospital. As to the length of time required, there may be a difference of opinion. Those who have observed are well aware of the fact that there are some men who require but little teaching; those, at the end of the first year, are better qualified than some of the others will ever be, no matter how long they are trained. The period of training under supervision should be at least three years in actual work with patients after at least two spent in reviewing the fundamentals, especially anatomy, physiology and pathology.

All surgeons know that it takes something more than a bright mind and strong desire to make a successful surgeon. Many an extraordinarily bright and well trained man has never been able actually to "make it go" successfully either in institutional or in private practice. There must be a natural aptitude for it.

A man taking graduate work in surgery should not be trained like a child. The opportunity ought to be afforded him to learn surgery, but that he should be "supervised" is to me ridiculous. Some of those having a good

deal to do with the graduate schools seem to think that surgery can be learned like Greek or Latin or history—so many hours, so many credits. Very bad is the idea that much more "credit" should be accorded a man for what is called "research" than for excelling as diagnostician, pathologist and practical surgeon. However, in the main it must be acknowledged that those engaged in teaching surgery are those who know it best and do it best.

USE OF RESEARCH

Research is, of course, most valuable, but a genius in research might be a failure as a surgeon. The best surgeons are those who know enough about research to enable them to increase their store of knowledge by intelligent experiments on the lower animals when, as and if the spirit moves them. It hasn't been so long since degrees in surgery were given for "original investigative work" extending over a period of six months to a year! Surgery cannot be learned in this way.

TRAINING GIVEN AT ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE

I wish to outline what we have been doing in our medical school and I should like to receive criticism, because I know, of course, that our plan is not perfect. The question is whether we shall be able to devise a better plan; by receiving criticism we shall at least learn some things not to do.

We began with a two year course twelve years ago, which has now been lengthened to four. A candidate must have creditably completed a rotating internship of one year. He begins his course in the department of pathology, where he must remain one year, applying himself to general pathology and to surgical pathology. If his work has been satisfactory to the head of the department of pathology, he enters his first year's hospital service.

In his first year's hospital service only two thirds of his time is given to the hospital, one third being spent in the anatomy, surgical pathology and experimental departments. He does no major operations on the human body during this year but he is first assistant in all but the most formidable operations; in these he must be second assistant. He is permitted to use the experimental laboratory and is furnished with materials. He experiments in acquiring technic. He is direct supervisor of the work of the intern.

His second year more or less repeats the first with the exception that this year, on pre-

Read before the St. Louis Surgical Society, Jan. 9, 1940.
Dr. Coughlin, who was professor of surgery and director of the surgery department of St. Louis University School of Medicine, died May 22, 1940.

senting a certificate of proficiency from the director of animal surgery, he is allowed to perform major operations on the human body if assisted by one of professorial rank. He may act as first assistant in any major case. In the most serious, such as operations on the brain, lung or stomach, he must be first assistant. In this year we use him during his school service as an instructor in anatomy and surgical pathology. He has the laboratory of technic at his disposal and must perfect himself in the technic of each major procedure before he will be permitted to perform it on a patient, even though assisted by the professor. We use him as an instructor for interns and for nurses. By the middle of this year he shall have completed a clinical study of his own choice, begun in his first month of hospital service and based on material that has passed through the hospital or outpatient department.

His fourth year of preparation is almost equally divided between hospital and school. He fixes his own schedule. He is given complete charge of four beds. It is up to him to keep the cases moving. His work is under the immediate supervision of the chief. He is, on request, entitled to the assistance of any one of professorial rank. He must not accept assistance of any one less than senior intern. In the last half of his service he does some animal experimentation and must present, at the end of his service, a thesis based thereon. His laboratory materials are furnished him without cost. We use him as a service supervisor, intern and extern instructor and, in the school, as demonstrator in anatomy and surgical pathology. He is expected to be able to pass a practical examination in anatomy, physiology, pathology and surgery at the end of the course.

We cannot yet know whether this is the best way to train surgeons. It will take fifteen or twenty years to decide the question. My opinion is that not all those who get such an opportunity will become surgeons, and many will yet become men of renown in surgery who will never have enjoyed such opportunities to learn it.

COMMENT

Has our method any advantages over the established method—that of learning through a long assistantship? Certainly the best way to qualify in the purely clinical aspects is the long period of assistantship with a master surgeon. But, as has been said before, master surgeons are rare. There are so many doing surgery in this country that the clinical material which falls to one man is not as abundant as formerly. Although there is greater need for a greater number of better qualified men, yet few can become master surgeons. These men whom we are turning out would make excellent associates

for well qualified surgeons until they become a few years older. These men, after all this training, are all under 30 years of age—some no more than 26. Surely this is too early an age for the acquisition of a surgical practice. Could it be better done in some other way?

Before he ever comes to learn surgery is the time for the prospective surgeon to learn medicine and people; he could do that in no better way than by going out into general practice at the end of his junior internship. Let him spend at least five years in this and then let him seek a course in general surgery, something like what I have outlined. It would require a certain "calling" in the candidate to go through with such a "proving." He would certainly have the necessary fortitude, and there are times in every surgeon's life when fortitude is a prize. Any young man who, having once established himself in private practice, is willing to "throw it all up" for an opportunity to study surgery for four years surely is willing to make a large sacrifice, and I believe that he would become a credit to his profession. The contention is that such a plan would take too long. Well, the young surgeon gets pretty well over being young before he gets much private surgical practice. He is not expected to get much practice of his own before he is 40. As it is, unless he is fortunate, I fear he must be often hungry and many times find his virtue sorely strained. No surgeon can be much credit to surgery these days unless he confines his attention to surgery. No one will enter surgery from now on except by the door of special training.

Beginning to Practice.—When you enter a new community, appearance is important. You do not have to have the most expensive clothes but what you wear can look well on you. Your car does not have to be new, but it can be respectable looking. Above all, cleanliness will make or lose a practice quicker than almost anything. After you have been out a few years, check yourself with your confrère as to whether you are keeping up to date. Have you attended meetings and read your medical journals? . . . As early as possible, become a member of your county and state society and meet with your fellow practitioners. Being charitable to the other doctor in your community is most important. . . . If you disagree with the other man's opinion, regardless of how bad his judgment has been, a kind interpretation of the case will make all happier, including the patient. Whenever possible, associate with men you have to look up to. This thought applies to business men as well as men in the profession. They are stimulating and will give you a subconscious lift. In your early practice associate yourself with dispensary services and charitable enterprises. It not only improves your knowledge but allows you to rub elbows with many people of value to you throughout your professional career. Always treat those in work associated with medical practice with kindness and respect. Although you will see doctors who will be unkind to nurses when they can't talk back, remember they have been taught to look up to you. See that they are able to.—Sproule, Ralph P.: *A Doctor Speaks to Students*, *Marquette M. Rev.* 5:1 (Nov.) 1940.

Digests and Reviews

GUY'S STUDENTS PASS EMERGENCY TEST

Slightly condensed from Guy's Hospital Gazette, Sept. 21, 1940.

Guy's Hospital has now been subjected to the effects of real modern warfare. The enemy has seen fit to indulge in indiscriminate bombing raids over the London area, and as a result we have received our share of casualties. On Saturday, September 7, in the late afternoon, a series of fires was started following an intensive air raid; using these fires as beacons, the raiders returned throughout the night to attack their military objectives or anything else in the very approximate neighborhood.

From the start of this offensive, a steady stream of casualties began to arrive at the Memorial Gates of Guy's Hospital. What we had organized and prepared for in the previous months had suddenly come to pass. Almost all of the patients were suffering from shock, a shock that was not only traumatic but also mental, for not a few of them had seen their relatives and friends fall victims to this German wretchedness.

Both medical and surgical staffs worked in complete harmony under the constant supervision of our deputy superintendent. The immediate problem in the majority of cases was the adequate administration of resuscitation. The architectural deficiencies of our buildings were easily overcome by the stable cooperation of the stretcher bearers, who worked ceaselessly and without complaint. This is not the time for a description of cases, but one cannot help remarking on the almost dramatic recovery of seemingly lifeless casualties after a vigorous regimen of resuscitation had been instituted. Many of these patients who had suffered a multiplicity of perforating wounds of the chest and abdomen together with head injuries and burns were removed to the operating room within a few hours of admission; there our surgeons operated on them, applying their tireless skill without effort and with admirable patience until their job was finished.

To avoid congestion of the wards by the accumulation of patients, a system of evacuation to base hospitals was started at once. Just as soon as emergency treatment had been applied and the patients had sufficiently recovered, they were comfortably accommodated in a stretcher bus, appropriate care being taken of the injuries so that patients did not suffer by transport. In spite of many of these operations taking place at night under constant exposure to bombs and shrapnel, there is not a single report of any patient having suffered adversely from the journey.

The performance of students and nurses throughout the entire procedure has been one of merit and a tribute to themselves and to Guy's Hospital. There was not the slightest suggestion of hysteria or fright among any of them, but, instead, each worked with a cool efficiency, applying his own intelligence to what had to be done instead of stupidly standing about waiting for orders. When there was work to be done there was always an abundance of available personnel ready on the spot; in the intervals between action, each person sought out a safe underground room and curled up in a well deserved quiet sleep.

Many months ago the student body was released from the Emergency Medical Service. At the time there was a good deal of speculation as to the reaction of the students, especially with regard to what might be expected of them when their services were really required. That question has now been answered; without thought to their personal safety, without bitterness or even a grumble, sleepless and fatigued as they were, they piled into each new task with a vigor that did them credit.

THE ANATOMIST IN MEDICAL EDUCATION

Abridgment of a lecture by Lewis H. Weed, professor of anatomy, Johns Hopkins University School of Medicine, Baltimore, delivered at Washington University School of Medicine, St. Louis, May 17, 1939, and published in the Journal of the Association of American Medical Colleges, September 1939.

I propose to discuss the field of anatomy in its broad relation to medical education. From the derivation of the word, anatomy would seem to be restricted to the cutting apart of finished total structures, but the subject matter studied by anatomists today extends far beyond the body structure of man and animals. To the time honored method of investigation through dissection with scalpel, probe, scissors and forceps, the anatomist has added to his tools of trade the microscope and microtome, the incubator and culture slide, the caliper and measuring rod, the kymograph and induction coil, even the spectroscope and colorimeter. Anatomy has evolved into a mother science which embraces certain well defined subdivisions—gross human anatomy, comparative anatomy, histology and cytology, embryology, neuro-anatomy and physiological anthropology.

Today a broadly extending academic discipline, this anatomy of medical schools has come to be one of the major biologic sciences that have to do with life processes as these affect the structure and to a lesser extent the function of vertebrates. The anatomist

remembers the position of his subject in the training of physicians up to a century or so ago, when practically the entire basic instruction of the young physician was centered in the dissecting table. The body of biologic fact was then all too small; yet out of anatomy grew physiology. With the development of the autopsy technic, gross morbid anatomy came from the dissecting table and soon assumed adolescence and adulthood as a separate university discipline.

EVOLUTIONARY CHANGES

The discovery of cells through the use of the compound microscope added its share of complications to the simple structure of medical education. While the anatomist was learning to use the microscope, the pathologist likewise was employing the same means toward unfolding the disturbances of structure caused by disease. Then, in the fourth quarter of the last century, medicine was advanced by the discovery of the relation of certain bacteria to disease, and medical education processes again had to accommodate themselves to a new subject in teaching. At the same time chemistry began to make its claims on the medical curriculum and, with the development of its biologic aspects, still another major discipline found its place in the required work of the ever suffering medical student. Almost simultaneously the study of materia medica became invigorated and altered through the introduction of chemical and physiologic approaches and a true pharmacology assembled a new mass of information, dislocating much of the old but retaining some of its classic learning. Even with these inroads into the curriculum there was plenty of time for all the required instruction in the four year course offered by the best American medical schools at the beginning of the century.

But how different it is today regarding the demand for required hours in the medical curriculum! We are still giving—and I believe properly—the degree of doctor of medicine at the end of the classic four year period. But, since the turn of the century, the total body of fact in medicine has increased enormously. Clinical medicine is no longer based entirely on pathology. During the past forty years chemistry, physics and physiology have contributed their full share to medical diagnosis, therapy and prognosis. The study of disease has broadened, to become rather paradoxically an investigation of the disturbances of physiology; of parasitism by bacteria, viruses, fungi and protozoan forms; of the biology of new growths. Alongside this development of internal medicine, the subdivisions of surgery have all undergone phenomenal growth.

These evolutionary changes have all occurred within subjects included in the medical course of fifty years ago. Yet other developments have

taken place in recent years, and the overcrowded curriculum of medical teaching is being pressed to include these also. Prominent in this group of new subjects is that of preventive medicine. And closely allied to this aspect there has come realization that medicine does not cease with determination of the diagnosis and therapy: that there are social, environmental, economic factors in disease which must be included in the summary of the patient as a sick individual. Then too industrial medicine, forensic medicine and medical genetics likewise have their many advocates; and the end is not yet in sight. Nor do we wish the end to come: we live in a field of advancing medicine and I pray that this pressure, embarrassing as it is to medical deans and curriculum committees, will never cease.

PURPOSE OF THE MEDICAL SCHOOL

What, then, should be the primary aim of the faculties of medicine which are responsible for the arrangement of the course of study leading to the degree of doctor of medicine in four years? The chief purpose of the medical school is to train physicians in the best possible way. Just what the faculty of medicine does in its course of instruction is in the final analysis determined by local opportunities, by local facilities, by the quality of the faculty and by the extent of financial support. The result is, in my opinion, most desirable, as it ultimately produces medical schools of widely diverging character. The aim of all these schools remains essentially the same—to train the best type of physician. If one adopts the contention that the chief aim of medical education should be the establishment of an attitude of mind toward the study of disease, the arrangement of the course of study and the general disposition of required and optional work become matters of relative indifference. The pattern of the curriculum is of secondary importance.

With such a concept of curricular patterns, we can view with calmness the constant reduction of required hours in courses like those in anatomy. The decrease in time allotted to anatomy seems the more striking as for many years anatomy formed almost the entire basis of preclinical instruction. For many generations anatomy had no real competitors in the struggle for the student's time.

SCOPE OF FOUR YEAR MEDICAL COURSE

Everywhere throughout medical schools today there is realization that in any of the prescribed divisions of instruction the student has time merely for an initial survey of the subject matter of that branch of medical knowledge. The fund of information is too large in every one of these subjects: the student can at best obtain merely the biologic philosophy of the subject, hardly the pertinent details. He learns in a preliminary way the manipulative procedures

employed in the field for the acquisition of knowledge, but the acquirement of technical skills is postponed in this educational process to the intern-resident years or to the years as laboratory assistant. Our four year medical course, therefore, becomes a preliminary canter across a wide and rugged field. The student acquires a general comprehension and a philosophy in each course rather than a great body of specific knowledge and a mastery of technical procedure.

The merit of this postponement of the acquirement of the technical proficiencies until the postgraduate years is that it has permitted medical teachers to devote their energies largely to presentation of biologic points of view rather than to insistence on technics. Here medicine has been more fortunate, or wise, than dentistry. For in American dentistry we are confronted with an art standing supreme in its international field as a health service. Dentistry is today a superb artistry, but only relatively few dental practitioners or teachers are aware of the full biologic implications of disease of the teeth and jaws. The dental schools of America have insisted that their students acquire in the four year curriculum all of the technical proficiency needed for immediate practice. The dental schools provide biologic courses in the preclinical medical sciences for roughly one and one half years of the four year course; then, in spite of sporadic efforts at reform, the school superimposes two and one half years of the most rigid technical discipline. No wonder that the scientific interests of the average dental student in the biologic and medical aspects of his great subject do not survive. The number of dental teachers who still maintain the spirit of investigative curiosity, except as to technical method, is woefully small. The result of the development of superb technics in dentistry has been a pulling away from medicine: dentistry has become too largely a restorative and reparative art. It has produced a technical perfection which is not being applied, and cannot be applied, to the whole population. Technical dentistry, therefore, has arrived in a blind alley: it can liberate itself as a health agency only by developing a biologic point of view and a biologic body of knowledge. To do this the dental school should emphasize the underlying biologic sciences and relegate technical training, except as to the theory of procedure, to postgraduate years. It would do well to follow medicine in its educational program.

MEDICINE A BIOLOGIC SCIENCE

Medicine is rapidly becoming more and more of a biologic science. The practice of medicine is still essentially an art, but alongside this art an appreciable body of scientific fact in human and mammalian biology is continuing rapidly to accumulate. As biologic information relating to

man is in the future assembled through the efforts of geneticists, biometrists, anthropologists, anatomists, physiologists, chemists and others, medicine will stand forth not only as a curative and preventive art but as a great division of human biology.

And in this future medicine the anatomist will retain the same place in medical education that he now occupies. The anatomist will continue to teach human morphology in its widest sense. Unquestionably, it will be a larger and more soundly based subject than the gross and microscopic anatomy of today; but it will still be aimed at the disclosure of man's structure.

In the future schools of medicine I look forward to the subjugation of technics and arts in medicine as a means toward an end; therapy and prevention will rest on a fundament of sound biologic information. In the future there will still be employment for the anatomist in medical education, still an opportunity for the anatomist to supervise the student's work on human structure, still the rare and priceless privilege for the anatomist to cultivate and encourage an intellectual curiosity in the medical student, and still problems requiring attack by the anatomist.

ANATOMY AND ITS SUBDIVISIONS

The field of future endeavor looms larger and more significant than it has in the past. While it may, in some laboratories, be unfashionable momentarily to work on the problems of gross anatomy, this subdivision of the science still presents a multitude of questions of fundamental moment. With new points of view, anatomists are returning to the great subject of variability in human structures to the study of racial anatomy.

But what of the other subdivisions of anatomy in the future? The nervous system will continue to demand the concentrated attention of anatomists. Correlational studies, relating structure to function, will probably still offer the best chance of profitable return. Various mammalian forms, representing special adaptations to functional needs in nature, afford splendid material for generations of earnest research. And possibly most fruitful of all will be the investigation of the anatomic and physiologic maturation of the nervous system.

The great field of endocrinology, in which stupendous progress has been achieved in recent years, will continue to attract the best efforts of anatomists. To the advance of the past twenty years the anatomist has contributed a large share, and it seems most likely that in cooperative endeavors with physiologists and biochemists the anatomist will continue to add an important factor in morphologic control. The potentialities of these phases of endocrine function are almost unexplored.

In embryology a tremendous opportunity lies ahead and we are just taking the first timid steps in an endeavor which a few years ago would have been impossible. The solution of the significant problems of implantation and early embryonic development will add a chapter to our knowledge of human growth. Today the field of chemical or physiologic embryology is opening up to new endeavors, and with the recently discovered weapon of radioactive chemical substances a wholly novel aspect of embryonic development and growth will be unfolded in a generation or two. Histology and cytology

are employing new means of attack on the chemical constitution of the cell. We have now the initial advances made by the methods of micro-incineration, of freezing drying fixation, of spectroscopic analysis, of quartz system spectrographic study with ultraviolet rays, and of the electron microscope.

It seems obvious that the anatomist has before him a great opportunity in research of prime importance to the understanding of structure. The anatomist has had a place in medical education; he will, I believe, continue to have one of the important roles in future medical education.

Comments

Dr. Nicholas Senn once said "A good surgeon is a good physician who operates."

In 1736 the first successful mastoid operation for suppurative disease was performed by Jean-Louis Petit (1674-1750). He was the foremost French surgeon of the early eighteenth century.

The first degree of doctor of medicine conferred on a woman in the United States was that received by Dr. Elizabeth Blackwell on Jan. 23, 1849, from the Geneva Medical Institution, affiliated with Hobart College, at Geneva, N. Y.

Dr. John B. Vernaglia, a surgeon at Medford, Mass., caught a tuna fish in Ipswich Bay, Mass., weighing 927 pounds, which is said to be a world's tuna fish record. The previous largest tuna fish, weighing 890 pounds, was caught by John Manning off Nova Scotia in 1939.

Since 1933 the number of women applicants to the freshman class of seventy-seven medical colleges in the United States had increased, the largest number being 689 in 1935, since which year there has been a gradual falling off in numbers. In 1939 the number of women applicants was 632, of whom 321, or 50.8 per cent, were accepted; in 1933, 62.3 per cent of the women were accepted.—Fred C. Zapffe, Secretary, Association of American Medical Colleges, Chicago.

Charles Robert Darwin, although an invalid for the rest of his life, labored for twenty years before publishing his great work "On the Origin of Species by Means of Natural Selection" (1859), perhaps the most wonderful piece of synthesis in the history of science. Darwin's extraordinary marshaling of facts, in evidence of the survival of the fittest by natural selection in the struggle for existence, had the same far-reaching influence on biologic speculation that the discoveries of Copernicus had on astronomy.—Fielding H. Garrison.

FOODS HIGHEST IN POTASSIUM

Bananas	Kohlrabi	Olives
Cabbage greens	Legumes	Paprika
Caviar	Lemons	Parsnips
Cereals	Lettuce	Pepper, black
Cocoa	Limes	Potatoes, white
Condensed milk	Meat extracts	and sweet
Dandelion greens	Meats and fish	Rutabagas
Dried fruits	Molasses	Splnach
Endive	Mushrooms	Truffles
Guavas	Mustard	Turnips
Honey	Nuts	
Horseradish		

FOODS LOWEST IN POTASSIUM

Apples	Cream	Milk
Asparagus	Cucumbers	Okra
Bacon	Eggplant	Onions
Berries	Eggs	Oysters
Bread, rye, white	Farina	Pears
Butter	Fruit juices (except	Peppers, green
Buttermilk	pineapple and	Pork
Cheese	tomato)	Rice, white
Citrus fruits	Grapes	Soup
Clams	Hominy	Squash, summer
Corn, green	Macaroni	Watermelon
Crackers		

—Bridges, Milton A.: *Dietetics for the Clinician*, ed. 3, Philadelphia, Lea & Febiger, 1937, reprinted here from Pattee, Alida Frances: *Practical Dietetics with Reference to Diet in Health and Disease*, Mount Vernon, N. Y., A. F. Pattee, Publisher, 1940.

DO YOU KNOW WHAT PHYSICIAN—

1. Was the first priest-physician of whom we have a record?

2. Was Ambassador from Great Britain to the United States?

3. By his discoveries in astronomy revolutionized science in general and established astronomy on a sound basis?

4. Invented a machine for unwinding the fiber of silk cocoons?

The answers are on page 1944

Correspondence

A SENIOR STUDENT VIEWS THE INTERNSHIP

To the Editor:—I should like to report the existence of a disease entity about which no literature has been written but which has existed since the birth of modern medical education. This disease is peculiar to medical students, is pandemic, beginning at the end of August (with the issuance of the "Educational Number" of THE JOURNAL) and lasting for an indefinite length of time, depending on two factors—"pull" and "resistance." Pathologically this is a disease of the psyche and runs a characteristic course. The onset is usually insidious, with prodromal symptoms of unexplained elation following third year final examinations in June. At the end of August, with the issuance of the aforementioned "Educational Number," the patient begins to feel overwhelmingly confused, undecided and unusually solicitous toward "friends" and professors. This is immediately followed by a period of undue overconfidence and grandiosity. During this period the individual closely resembles the schizophrenic, for he is continually building hospitals in his mind and living gloriously in them. On November 15, there is a sudden and marked state of depression, disorientation and confusion. This also lasts for an indefinite period of time, but sooner or later the individual returns to normal. However, there are certain sequelae which leave a definite impression on the individual's personality. Treatment, of course, is a satisfactory internship.

This brings me to the main thought of my letter, namely that procurement of internships is as bad as ever. This should not be so, for to me this matter is a simple one, revolving around two basic factors:

1. Hospitals want interns.
2. Students want internships.

However, there is a conflicting element in that some of the larger hospitals do not recognize the graduates of some of the less publicized schools. Therefore, when a student applies at these hospitals he is unmindful of this condition. With ignorant hope he wastes precious time which he could have used to better advantage by applying at a more sympathetic hospital. Consequently, I should like to submit this plan for your consideration. The plan is as follows:

1. Each hospital approved by the American Medical Association as found in your educational number is to receive each year on a definite date a list of approved grade A medical schools.
2. From this list each hospital is to pick a number of medical schools from the graduates of which it will entertain applications for internships.
3. These choices are to be sent to the American Medical Association, and this information is to be rearranged in such a manner that each school will know which hospitals will consider the applications of its students.
4. At the beginning of each school year each medical school will post a list of those hospitals which have expressed their willingness to receive applications from that particular school.
5. Appointments are to be made on November 1 by telegram, and each appointee is obligated to accept or refuse by telegram within twenty-four hours.

6. All hospitals that by the end of the following day still have vacancies are to report the number of vacancies to the American Medical Association.

7. A list of vacancies is to be compiled and sent to each medical school no later than November 15.

From this sketchy outline several advantages can be seen. First, and most important, the student who has no "pull" will not waste his time trying to get into a hospital where he has no chance at all. However, this does not prevent the student from trying to get into a hospital which is not on his school's list. Finally, the student after being rejected will now know which hospitals still have vacancies.

For those of us who are trying to obtain an internship this is a real problem. I submit this letter in good faith, with the hope that if this plan is not acceptable it will inspire other suggestions and further effort to remedy the present deplorable situation.

GEORGE SPECK, Washington, D. C.

FIRST SUCCESSFUL CESAREAN SECTION

To the Editor:—Under comments in The Student Section, bottom of page 1505 of the October 26 issue of THE JOURNAL, in regard to the operation by Dr. Richmond you state "The operation was done in Middletown, Ohio, in 1827. . . ."

The operation was performed just east of Cincinnati at Newtown, Ohio, on a servant of one of the early settlers of the Little Miami River Valley.

In 1912 the McDowell Medical Society of Cincinnati erected a monument in the memory of Dr. Richmond and of the first successful cesarean section in the United States, which he performed April 22, 1827.

JOHN T. CRONE JR., M.D., Milford, Ohio.

EDITORIAL NOTE.—According to Blanton in his "Medicine in Virginia in the Eighteenth Century," published by Garrett and Massie, Richmond, 1931, the first cesarean section in America was performed by Dr. Jesse Bennett on his own wife in a frontier settlement in the Shenandoah Valley in Virginia in 1794, which was thirty-three years earlier than that by Dr. John Lambert Richmond, to which Dr. Crone refers in his communication. Blanton writes: Mrs. Bennett's "labor was a difficult one owing to a contracted pelvis, and Dr. Alexander Humphreys of Staunton was called in consultation. The doctors tried forceps without success. Between the alternatives of craniotomy and cesarean section the patient chose the latter in spite of the opposition of Dr. Humphreys and his persistent refusal to perform such a dangerous operation. The case was urgent, and Jesse Bennett decided to operate himself. The patient, stretched on a crude plank table over two barrels, was put under the influence of a large dose of opium. Assisted only by two Negro women, the courageous frontier surgeon by one quick stroke of the knife laid open the abdomen and uterus and quickly delivered child and placenta. At this stage he delayed long enough to remove both ovaries. . . . The wounds were closed with a stout linen thread, and contrary to the expectation of every one present Mrs. Bennett was soon well and active. The child, a daughter, lived to be 77 years of age." It is

interesting to note that the oophorectomy performed on his wife by Dr. Bennett antedated Ephraim McDowell's famous operation on Mrs. Crawford by more than fifteen years. Dr. Bennett has not generally been given a place of honor in the medical history of

America, because he did not report his case in a medical journal. Dr. John Lambert Richmond reported his operation in Newtown, Hamilton County, Ohio, in February 1830 (*Western Journal of the Medical and Physical Sciences* 3:485).

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items for consideration for publication in the Student Section.

First Aid Required of Minnesota Freshmen

The University of Minnesota Medical School, Minneapolis, has instituted a required course in first aid for freshman medical students. The one quarter course, consisting of fourteen lectures and six practical demonstrations, was instituted because it was felt that it was pertinent to the preparedness program in the event of an emergency. This is one of the first medical schools in the country to include such a course in the curriculum for freshmen.

Student on Orthopedic Program

Marshall R. Urist, a senior at Johns Hopkins University School of Medicine, represented undergraduate research at a meeting of the Robert Jones Orthopedic Club in Baltimore, November 7; his paper was entitled "Research in Calcification of Callus." There were papers also by Dr. Walter Dandy on "Intraspinal Causes of Back Pain" and by Dr. Warfield Firor on tetanus, and Dr. M. N. Smith-Petersen showed a movie on arthroplasty.

Vermont Lengthens the Senior Year

The office of the dean of the University of Vermont College of Medicine, Burlington, has announced that beginning next June 1 the teaching in the senior year of the medical college will be extended from thirty-two weeks to forty-four weeks.

Michigan Reduces Number of Prescribed Hours

Recognizing the value of independent thinking and self-conceived effort, the University of Michigan Medical School, Ann Arbor, has reduced the number of prescribed hours in the curriculum. The total number of hours required for didactic courses, clinics and laboratory sciences had become so great that students found no time for independent study and reflection. According to Dean Albert C. Furstenberg, medical training is not the accumulation of factual knowledge and information; it is the acquisition of understanding and powers of interpretation which gives the student a grasp of the practical problems.

Alpha Omega Alpha at Western Reserve

The following students of Western Reserve University School of Medicine, Cleveland, have been elected to Alpha Omega Alpha honorary medical society: Norma Anderson Beall, Daniel Anthony Brody, Janet Turreff Dingle, Gerald Tambling Kent, Aaron Paley, Leonard Michael Schuman, Joseph Selman and Lester Louis Williams.

Guest Speakers at Oklahoma

Dr. Alfred W. Adson, professor of neurosurgery at the Mayo Foundation, Rochester, Minn., addressed the entire student body of the University of Oklahoma School of Medicine, Oklahoma City, in October on "The Future of Medical Practice"; Dr. Elliott P. Joslin,

emeritus clinical professor of medicine, Harvard Medical School, Boston, on "Diabetes," and Dr. M. Edward Davis, associate professor of obstetrics and gynecology, University of Chicago School of Medicine, addressed the senior class on the use of stilbestrol. The addresses were delivered during the time of the meeting of the Oklahoma City Clinical Society, October 28-31.

New York University's Freshman Officers

The first year class at New York University College of Medicine, New York, has elected the following officers: president, John G. Murray of Brown University and Mount Vernon, N. Y.; vice president, Edward E. Banta of Dartmouth and Tenaflly, N. J.; treasurer, Sheldon Schwartz of Rensselaer Polytechnic Institute and Richmond Hill, L. I., N. Y.; secretary, Naomi de Sola Pool of Goucher College and New York; council representatives are Sidney A. Haber of Cornell and New York and Franklin Brundage of Cornell and Pelham Manor, N. Y.

Virginians Honor Yellow Fever Volunteer

John J. Moran was guest of honor at a dinner given by the faculty of the University of Virginia Department of Medicine, Charlottesville, October 23, at which the principal speaker was Brig. Gen. Jefferson R. Keane, U. S. Army, retired. Mr. Moran was one of twenty-three volunteers who contracted yellow fever in the famous experiments conducted in Cuba by the U. S. Army Yellow Fever Commission in 1900 and 1901, of which Major Walter Reed was chairman.

President Theodore Roosevelt transmitted to the Congress of the United States, Dec. 5, 1906, a memorandum addressed to him by Surgeon General O'Reilly, which listed the volunteers who had submitted to the yellow fever experiments in Cuba and had the following to say concerning Mr. Moran:

Conspicuous among them was John J. Moran, a civilian clerk employed at the headquarters of Gen. Fitzhugh Lee, at Quemados, who was one of the earliest volunteers for the second set of experiments, and whose action was dictated by the purest motives of altruism and self devotion. Mr. Moran disclaimed, before submitting to the experiments, any desire for reward and has never accepted any since, although he was offered the \$200 which the liberality of the military governor enabled the commission to give to each experimental patient, the members of the board excepted. Such was his modesty that he has made no effort, so far as known to this office, to make known his connection with these experiments and reap the credit which is so justly due him. Mr. Moran was a native of Ohio.

Utah Dissolves Medical Fraternities

The students of the University of Utah School of Medicine, Salt Lake City, recently voted to dissolve the medical fraternities and establish a medical student association. The first activity scheduled by the new association is to sponsor the annual medic-lawyer football game and the dinner dance which follows. John Bruce Balken '43 was elected president of the new organization; Norman S. Anderson '44, vice president, and Miss Denise T. Callister '43, secretary and treasurer.

Expenses at Tennessee

For Tennessee students, the expenses at the University of Tennessee College of Medicine, Memphis, amount to between \$225 and \$275 a quarter. The cost to students from other states is \$50 more. Tuition per quarter is \$70 for Tennessee students and \$120 for out of state students. A contingent deposit is maintained at \$15. Living expenses, supplies and books account for the remainder. Students are required to have a microscope, and in the second year a hemocytometer, hemoglobinometer, a blood lancet and a stethoscope.

Scholarship Awarded at Texas

Mr. Blocker H. Joslin '41 has been awarded the J. B. Kass Research Scholarship in Preventive Medicine at the University of Texas Faculty of Medicine, Galveston. The scholarship is awarded to a medical student selected by a committee comprising a faculty member, a representative of the student body nominated by the student's association and a representative of Dr. Kass. The purpose of this yearly scholarship is to encourage research in preventive medicine.

Growth of Louisiana's Library

The library of the Louisiana State University School of Medicine, New Orleans, is known as the Agramonte Memorial Library, in honor of Dr. Aristides Agramonte, who was a member of the U. S. Army Yellow Fever Commission, which conducted experiments in Cuba in 1900 that led to the discovery of the method of transmission of yellow fever. Dr. Agramonte was appointed professor of tropical medicine in 1931 at Louisiana State University School of Medicine but died shortly before the opening of school in that year. The Agramonte Memorial Library has just closed a successful year, during which a new workroom was added to the library, the stack space was doubled and a number of journal files were completed, bringing the total of complete files of journals in the library to seventy-eight. The library had at the close of the fiscal year 10,885 volumes, an increase of 20 per cent for the year. The circulation increased 7 per cent.

New A. O. A. Members at Emory

The following members of the senior class at Emory University School of Medicine, Atlanta, Ga., were elected last month to membership, based on scholarship, character, leadership and achievement, in the honorary fraternity Alpha Omega Alpha: William Rhett Craig, Walhalla, S. C.; Manne Adams, Sebring, Fla.; William Evans Goodyear, Emory University, Ga.; Charles Thornton Cowart, Danaldsville, Ga., and Cecil Glenn White, Tucapaw, S. C.

"Dad's Day" Banquet

More than 600 persons attended the banquet, October 12, at the State University of Iowa, Iowa City, in honor of the students' fathers. The toastmaster on this occasion was medical student John M. Rhodes '41, a member of Alpha Omega Alpha and of A. F. I., an honorary fraternity for outstanding senior students of all the colleges at the university.

College of Medical Evangelists

The juniors and seniors of the College of Medical Evangelists, Los Angeles, were addressed November 7 by Dr. Walter C. Alvarez of Rochester, Minn., on "Abdominal Pains," a lecture which, our correspondent writes, was essentially on the art of medicine. In attendance also were the interns of the Los Angeles

County Hospital, students of the University of Southern California School of Medicine and members of the faculty of these institutions.

The 298 students enrolled in the College of Medical Evangelists came from thirty-eight states, the District of Columbia, and the following foreign lands: Australia, Bermuda, British West Indies, Canada, Canal Zone, China, Dutch East Indies, England, Germany, Hawaii, Iceland, India, Iran, Iraq, Korea, Palestine, Peru, Philippine Islands, Puerto Rico, Scotland, South Africa, Switzerland, Trinidad and Turkey.

Harvard Students After Twenty-Five Years

A celebration was held in Boston in June by members of the class of 1915 of Harvard Medical School which was attended by forty-one of the eighty-four members of the class still living. Four men came to the celebration from California, two from Colorado and two from Missouri. The class met in the faculty room of Harvard Medical School to be addressed by A. Lawrence Lowell, president emeritus of Harvard University, Prof. Walter B. Cannon, Prof. Cecil K. Drinker and Dean Burwell. The next day the classmates visited the hospitals. Saturday afternoon the classmates and wives assembled for luncheon and class pictures, then motored to Harvard, Mass., to be entertained in the country home of one of their members. The class of 1915 contributed \$1,450, which was turned over to the dean for the use of the medical school.

Temple's Class Officers

John H. Kolmer was elected president of the class of 1943 and David P. Osborne president of the class of 1942 at the recent elections of the freshman and sophomore classes of Temple University School of Medicine, Philadelphia.

"DO YOU KNOW WHAT PHYSICIAN"

Following are answers to the questions appearing on page 1941:

1. Imhotep, who lived about 3,000 B. C. He was the most influential man in Egypt at that time. Imhotep gave such an impetus to medicine that about 700 years later it had become well organized. Temples of healing were built throughout Egypt in his honor. He was a real person and held the same place in Egyptian medicine that Aesculapius, a mythological character, held in Greek medicine. Imhotep was also the architect and builder of the first Egyptian pyramid.

2. Sir Auckland Campbell Geddes, who was professor of anatomy first at Edinburgh, then at the Royal College of Surgeons, Dublin, and afterward at McGill University, Montreal.

3. Nicholas Copernicus (1473-1543). Copernicus, a native of Poland, received his degree of doctor of medicine from the University of Cracow. After studying the motion of the heavenly bodies for years, he published in 1543 his treatise on the revolution of planets around the sun, giving proof that the sun was the center of the universe, rather than the earth.

4. Dr. Thomas H. Chivers (1809-1858). Dr. Chivers received his M.D. degree from Transylvania University (now the University of Kentucky) in 1830. He never practiced medicine as a means of livelihood, but throughout his life he practiced free of charge for those unable to pay. His chief interest was literature and his writings make several large volumes. There was a strong similarity between his style and that of Edgar Allan Poe. Dr. Chivers was awarded a prize at one of the fairs in his state for inventing a machine for unwinding the fiber of silk cocoons.

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SURGICAL CORRECTION OF HORSESHOE KIDNEY

CHAIRMAN'S ADDRESS

FREDERIC E. B. FOLEY, M.D.

ST. PAUL

The anomaly horseshoe kidney, apart altogether from accompanying renal pathologic change, presents a clear-cut and definite clinical problem. It is the problem of what may be called horseshoe kidney disease as distinct from disease of the horseshoe kidney.

The literature abounds in reports of the occurrence of the anomaly horseshoe kidney and in descriptions of its morphology and autogenesis. There is an abundance of clinical reports dealing with disease of the horseshoe kidney. They recount occurrence of all the ordinary renal lesions such as hydronephrosis, pyonephrosis, stone, tuberculosis and neoplasm, found in association with this extraordinary form of kidney. Some of the reports speculate concerning the anomaly as an etiologic factor in occurrence of the associated lesion. In all but a few reports, to be mentioned in detail later, the anomaly has not been held directly responsible for the symptoms present and no attempt has been made to eliminate it as an etiologic factor by restoration of normal anatomic relationships. They are simply reported cases of common renal lesions occurring in an uncommon anomalous kidney. Such cases do not touch on the clinical problem of the anomaly itself—that is, the problem of relieving the painful and other symptoms caused by the anomaly and preventing or arresting pathologic changes that may insidiously accompany it.

A horseshoe kidney not affected by any significant pathologic change apart from the anomaly may be productive of symptoms demanding relief. With the exception of only a few reported cases, surgeons have failed to accord this relief and apparently have failed to contemplate the surgical problem of doing so. It will be shown by the personal cases here reported and by analysis of other cases reported in the literature that surgical correction of the anomaly by division of the isthmus and nephropexy on one or both sides is capable of restoring normal relationships and relieving the subjective symptoms that may be caused by the anomaly.

With the exception of twelve cases reported prior to 1930, when the present thesis had its inception, and six cases reported since then, all clinical reports have neglected this particular and very important phase of horseshoe kidney disease. This cannot be said of

Gutierrez's monograph "The Clinical Management of Horseshoe Kidney,"¹ published in 1934. Gutierrez originated the term "horseshoe kidney disease" to distinguish cases of the anomaly not associated with significant pathologic change from cases in which concomitant disease of the malformed kidney is present. It is a useful and descriptive term and should be retained.

Although not supported by the results of personal experience, Gutierrez concluded that horseshoe kidney per se without any accompanying renal lesion of significance is capable of causing subjective symptoms and that these should be amenable to relief through surgical restoration of normal relations—that is, operative division of the fused kidneys and their restoration to normal positions.

Prior to Gutierrez's publication in 1934 I had already embarked on the same thesis by another avenue—trial of the operation. In 1935 a preliminary report² described the early results of this operation in five cases in which there was no significant pathologic change apart from some degree of the pelvic dilatation that usually accompanies the anomaly. The present address as chairman of your section will report my personal experience with this procedure in seven such cases, recount the end results in them and indicate the conclusions that may be drawn from them and the nineteen similar cases reported in the literature.

Any outspoken pathologic change in the horseshoe kidney that is wholly responsible for the symptoms present provides the same clearcut and definite indications for correction of the lesion that the same lesion would provide in the normally formed kidney. As already indicated, such cases of horseshoe kidney associated with outspoken pathologic change do not enter the present considerations. However, with few exceptions reports in the literature indicate that in the consideration and management of horseshoe kidney the associated lesion has merely been assumed to be wholly responsible, has overshadowed the anomaly and has been the sole object of clinical attention and surgical attack, while the anomaly itself and its evils have been almost wholly neglected. This does not prove or admit that in such cases the anomaly is not just as important as the common renal lesion accompanying it or even that the anomaly may not have been responsible for development of the lesion present. To distinguish between cause and effect in any relationship that exists between the anomaly and the lesion associated with it is not my purpose here. The thesis deals only with horseshoe kidney per se as a clinical problem and does not touch on the problems presented by concomitant pathologic change.

Dr. Harry A. Wilmer rendered assistance in the search for references and prepared the accompanying bibliography and case summaries.
Read before the Section on Urology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Gutierrez, Robert: The Clinical Management of Horseshoe Kidney, New York, Paul B. Hoeber, Inc., 1934.
2. Foley, F. E. B.: Minnesota Med. 18: 176-182 (March) 1935.

THREE GROUPS OF CASES OF HORSESHOE KIDNEY

For the present purpose all cases of horseshoe kidney may be divided into three groups and commented on as follows:

GROUP 1.—*Cases of horseshoe kidney without renal pathologic change or symptoms of renal origin.* In the majority of clinically recognized cases belonging to this group the urologic investigation leading to discovery of

the anomaly is prompted by painful abdominal symptoms of other than renal origin. In a large minority of cases the investigation is prompted by the patient's own discovery of an abdominal mass representing the isthmus of the horseshoe kidney or by the physician's similar discovery. In a small minority of cases belonging to this group the coincidence of urinary symptoms of vesical or urethral origin, not related to the upper

TABLE 1.—*Summary of Cases of Symphysiotomy for Horseshoe Kidney Reported in the Literature*

Case	Author and Year	Sex, Age	Clinical Data	Operation	Comment
1	Martinow, ³ 1910.....	♀ 40	Pulsating sensation in abdomen since childhood; pain above umbilicus of 4 years' duration; constipation; severity and frequency of pain increased; palpable mass	Chloroform anesthesia; transperitoneal approach; tumor found to represent horseshoe kidney; isthmus separated from aorta and divided; kidneys separated	Diagnosis by palpation: result, 5 months' complete relief
2	Rovsing, ³ 1911.....	♂ 23	Lower abdominal pain for 5 years occurring in attacks of sudden onset and lasting 3 hours; all attacks induced by activity; palpable mass moving with respiration	Transperitoneal approach; isthmus divided; separated left kidney retracted into normal position	Diagnosis by palpation under anesthesia; result, early complete relief
3	Malinowsky, ³ 1912.....	♀ 28	Persistent abdominal pain; hyperacidity; palpable mass	"Isthmus crushed"	Complete relief of pain; hyperacidity not relieved; result, early complete relief
4	Brongersma, ³ 1914.....	♀ 37	Since childhood bilateral lumbar pain more severe on left; later lower abdominal pain; left-sided colic; 2 attacks of bilateral pyelitis treated by lavage; previous operation for calculus; calculus not found; uterus and tubes removed	Transperitoneal approach; isthmus divided; kidneys retracted from midline	Result, 2 months "felt well"
5	Brongersma, ³ 1919.....	♂ ?	Pain in region of umbilicus; hematuria on 1 occasion following heavy lifting	Transperitoneal approach; isthmus divided; urinary fistula treated by nephrostomy	Diagnosis by operation: result early complete relief.
6	Kroiss, ³ 1922.....	♀ 29	Attacks of severe abdominal pain for 10 years; severe bilateral lumbar pain radiating to umbilicus occasioned by heavy lifting; pain relieved by flexion of spine, increased by lifting, coughing and sneezing	Transperitoneal approach; isthmus resected	Result, permanent complete relief
7	deGroot, ³ 1922.....	♂ 16	Attacks of abdominal pain of increasing severity 2 years; palpable mass	Transperitoneal approach; isthmus divided	Result, "recovery"
8	van Houtum, ³ 1922.....	♀ 37	Attacks of severe colicky lumbar and abdominal pain 1½ years; hematuria; pain and hematuria induced by exercise disappeared on rest; diagnosis by palpation under anesthesia, confirmed by pyelography	Transperitoneal approach; isthmus divided	Result, permanent relief
9	Kidd, ³ 1923.....	♀ 32	Lumbosacral pain in increasing severity for 4 years; pain increased by exercise; also occurred when lying down; partially relieved by lying on right side; previous operation with discovery of horseshoe kidney	Transperitoneal approach (3 months following previous operation); tense isthmus lying against aorta; isthmus divided; both kidneys retracted	Result, postoperative death on 5th day
10	Judd, Bransch and Scholl, ⁴ 1922	♀ ?	Not stated	Hydronephrosis; "... isthmus was divided and the diseased kidney rotated in order to permit the ureter to lie in normal position"	Result, 18 years of complete relief (personal communication)
11	Eggers, ³ 1922.....	♂ 18	Former period of vague right-sided pain of 10 years' duration followed by relief; 12 weeks prior to observation, sudden attacks of severe left-sided colic followed by passage of stone; recurrence of pain; palpable mass	"Left flank incision"; removal of stone; isthmus divided; left nephropexy	Diagnosis by operation: result, "recovery"
12	Papin, ³ 1922.....	♀ 32	Lumbar and abdominal pain of gradually increasing severity; palpable mass; diagnosis by pyelography	Extraperitoneal approach; division of isthmus	Result, early complete relief
13	Mintz, ³ 1925.....	♀ 33	Recurrent attacks of poorly localized pain; large palpable mass	Transperitoneal approach; division of isthmus	Diagnosis by operation: result, early complete relief
14	Lynch and Thompson, ⁵ 1934	♂ 36	"Backache" and pain referable to left kidney; relieved by lying down; pain referable to both kidneys of increasing severity for 15 days; tenderness in both flanks	Retroperitoneal approach; division of isthmus; division of anomalous vessels	Diagnosis by pyelography (?): complete relief of left-sided pain; right-sided pain improved; result, 3 months as noted
15	Chwalla, ⁵ 1935.....	♀ 29	Bilateral lumbar and umbilical region pain induced by heavy lifting of 4 years' duration; "abdominal colic" since childhood, recently more frequent; loss of appetite; pulsation in umbilical region; slept in semi-erect position for relief of pain	Transperitoneal approach; resection of isthmus	Result, 14 years of complete relief
16	Chwalla, ⁵ 1935.....	♀ 31	Abdominal and lumbar pain since childhood induced by extension of spine; attacks of great severity; palpable, very movable mass identified as horseshoe kidney	Transperitoneal approach; division of isthmus	Diagnosis by pyelography (?): result, 10 years of complete relief
17	Baker and Colston, ⁵ 1936	♂ 30	Intermittent right lumbar pain for 7 years, relieved by lying down	Extraperitoneal approach; division of isthmus; right nephropexy	Result, early complete relief
18	Baker and Colston, ⁵ 1936	♂ 52	Attacks of severe right lower quadrant pain for 1 year; right renal calculus	Extraperitoneal approach; division of isthmus; right pelvolithotomy; right nephropexy	Diagnosis by pyelography: result, early complete relief
19	Strode, ⁵ 1939.....	♂ 25	Abdominal pain for 6 years; tenderness in left kidney region; appendectomy 3 years previously without relief	1. November 1936, left retroperitoneal approach; resection of lower pole of right kidney; right nephropexy (?)	Diagnosis by pyelography: result, early complete relief

urinary tract, has indicated the urologic investigation leading to discovery of the anomaly.

In cases of this group the horseshoe kidney is of clinical importance only in a negative way. Since it is not affected by pathologic change and causes no symptoms, there is no more reason for surgical intervention with such a horseshoe kidney than there is reason to intervene surgically with an undiseased and symptomless kidney of normal form. The anomaly itself is of no surgical importance. In this group of cases the clinical burden is to discover the nonrenal cause of symptoms, if symptoms are present, and avoid the error, and possibly needless surgery, of assigning the anomalous though innocent horseshoe kidney as the cause of symptoms.

GROUP 2.—*Cases of horseshoe kidney with outspoken renal pathologic change and symptoms of renal origin.* Under competent medical care and modern methods of urologic diagnosis most cases of this group are clinically recognized, both the anomaly and associated lesion being clearly demonstrated. In most cases the associated lesion presents the same diagnostic and surgical problems that the same lesion would present in the normally formed kidney. These problems are made peculiar by presence of the anomaly, but the importance the anomaly may have beyond this has been largely neglected. A large majority of the reported cases of horseshoe kidney belong to this group. The associated lesions have been of great variety and include almost all of the common surgical renal lesions such as hydronephrosis, pyonephrosis, stone and tuberculosis.

In many cases of this group surgical correction of the "common renal lesion" associated with the anomaly is only one part of the problem present. Often it is found that correction of the lesion associated with the anomaly does not serve completely to right the evil. If the anomaly has been an etiologic factor in occurrence of the lesion its continuing presence may lead to recurrence of the lesion. If the symptoms have been due wholly or partly to the anomalous relationships they will not be completely relieved without surgical correction of the anomaly. Conceivably hydronephrosis occurring in association with horseshoe kidney may not be due to mechanical obstruction occasioned directly by the anomaly but instead to stricture, aberrant vessel or other form of obstruction not caused by the anomaly. Surgical correction of such an obstruction without correction of the anomaly should give complete relief provided the anomaly per se plays no part in the production of symptoms. The fact is, however, that most cases of hydronephrosis occurring in association with horseshoe kidney are due directly to mechanical obstruction made by the horseshoe kidney itself. This type of obstruction will be further considered in the comments concerning the cases of group 3.

In many cases of this group an unsatisfactory result of operation is recognized but there has been habitual failure to recognize that continuing presence of the anomalous relations and failure to correct them surgically are responsible for the unsatisfactory outcome.

In this combination of an outspoken renal lesion associated with horseshoe kidney it may be difficult or impossible to say what part of the symptom complex is caused by the lesion and what part is caused by the anomaly. Unless there are good indications to the contrary, it may be best in such cases to proceed on the

assumption that the associated lesion is solely responsible, surgically correct it and leave the anomalous relationships undisturbed. Should an unsatisfactory result ensue, the responsibility of the anomaly for it should be investigated, and if good indications are found the anomalous relationships should be corrected by division of the isthmus and normal positioning of the separated kidneys.

GROUP 3.—*Cases of horseshoe kidney with symptoms of renal origin but without renal pathologic change other than some degree of pelvic dilatation.* The cases of this group are the ones most intimately concerned in the present thesis.

There is good reason to believe that a large number of cases of horseshoe kidney belong to this group—and yet with few exceptions nothing has been done about them. They have been nearly like the weather: every one talks about the weather but no one does anything about it.

Many cases of horseshoe kidney with pyelograms showing no significant departure from normal except for the anomaly are recognized clinically and many of them have been reported. They may belong to group 1, in which the anomaly is not the cause of pain or any other clinical manifestations whatever. As already indicated, such cases are of no clinical importance. However, in many cases belonging to this group the malformation itself is directly the cause of pain and other symptoms, which prompt investigation, leading to discovery of the anomaly.

If symptoms are present, the burden of proof goes with saying they are not caused by the horseshoe kidney. This is particularly true when the symptoms are suggestive or typical of renal origin. However, it appears that the horseshoe kidney without any significant pathologic change may cause vague and indefinite symptoms not suggestive, and by no means typical, of renal origin. Gutierrez emphasizes this point. Among these symptoms are vague abdominal pain or "belly ache," constipation and other digestive disturbances.

From personal experience I am not familiar with such cases, for in all the cases here reported in support of the present thesis symptoms typical of renal origin were present.

Nor can I say from personal experience that absence of significant pathologic change properly defines this group of cases. In some of the cases here reported there was obvious pathologic change in the form of pelvic dilatation while in others the pyelogram after operation has shown disappearance of what was originally considered insignificant dilatation of the pelvis in the preoperative pyelogram. In the light of this change in response to operation it becomes obvious that the slight dilatation present before operation in these cases actually should have been regarded as significant.

My own observations in the personal cases here reported make it appear certain that the various degrees of pelvic dilatation usually present in cases of this group are due directly to mechanical obstruction of the ureters occasioned by the anomaly: abnormal insertion of the ureter into the pelvis and contact of the ureter with the isthmus. These malrelationships were clearly evident in every case. The pelvic dilatation present varied from insignificant dilatation to outspoken hydronephrosis (case 5). Even in the latter case no other possible cause of obstruction could be found. The

dilatation, whatever its degree, regularly diminished in response to surgical restoration of normal relationships of the ureter.

However, in the literature and particularly in the monograph of Gutierrez are found reports of cases with

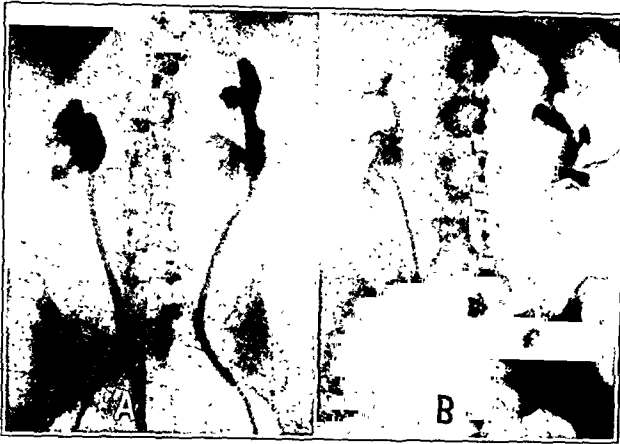


Fig. 1 (case 1).—A, preoperative right and left pyelo-ureterograms; B, postoperative right and left pyelo-ureterograms.

pyelograms showing no deformity whatever suggestive of pathologic change apart from the anomaly but presenting either symptoms typical of renal origin or vague symptoms possibly of renal origin. To determine surgical indications, if any, in the latter cases is a difficult problem. If comprehensive investigation fails to disclose an extrarenal lesion capable of causing the vague symptoms then there is much reason to believe that the symptoms will be relieved by correction of the anomalous relations, by division of the isthmus and nephropexy on one or both sides.

PROPER CLINICAL MANAGEMENT OF HORSESHOE KIDNEY

In the foregoing discussion a problem concerning the clinical management of horseshoe kidney has been posed. The comments made anent the matter already



Fig. 2 (case 2).—A, preoperative right and left pyelo-ureterograms; B, postoperative bilateral pyelogram.

have indicated the chief conclusion to be drawn. That conclusion is:

The anomaly horseshoe kidney not affected by concomitant pathologic change of significance may be productive of painful and other symptoms and insidious development of renal disease and can be restored to normal anatomic relations with relief

of symptoms and arrest of the insidiously developing renal disease by appropriate surgical intervention—symphysiotomy and nephropexy.

This conclusion is based on cases reported in the literature and the personal cases to be reported here.

Prior to 1930 when the first personal case was encountered there had been reported in the literature only twelve cases of horseshoe kidney in which symphysiotomy with or without nephropexy had been made.³ All of these were in Europe and in all save one, the case of Papin, operation by the transperitoneal approach was done. Unfortunately the eventual end results in these cases are not described, but the immediate symptomatic result was reported as excellent in all of the eleven surviving patients.

In a paper dealing with renal anomalies in general published in 1922, Judd, Braasch and Scholl⁴ mention but do not otherwise report a case of horseshoe kidney in which the isthmus was divided and "the right portion of the divided kidney was rotated in such a way as to make the ureter lie in its normal position." By personal communication it is learned from Dr. Braasch



Fig. 3 (case 3).—A, preoperative right and left pyelo-ureterograms; B, postoperative excretion urogram.

that eighteen years after operation this patient was alive and well, the result of operation appearing to be excellent.

The twelve European cases and the case of Judd, Braasch and Scholl, all reported prior to 1930, appear as cases 1 to 13 inclusive in the cases of symphysiotomy for horseshoe kidney reported in the literature summarized in table 1.

Since 1930, when the series of personal cases was started, there have been reported in the literature six more cases of this sort.⁵ The results in three cases are

3. The twelve cases were reported by:

- Martinow, A.: *Zentralbl. f. Chir.* 9: 314, 1910.
- Rovsing, Thorkild: *Ztschr. f. Urol.* 5: 587-601, 1911.
- Malinowsky, J.: *d'urolog.* 1: 869, 1912.
- Brongersma, H.: *Ztschr. f. Urol.* 8: 470, 1914.
- Brongersma, H.: *J. d'urolog.* 8: 425, 1919.
- Kroiss: *Verhandl. d. deutsch. Gesellsch. f. Urol.*, 1922.
- deGroot, S. B.: *Ztschr. f. urol. Chir.* 8: 170, 1922.
- van Houtum, G.: *ibid.* 8: 165-169, 1922.
- Kidd, Francis: *Proc. Roy. Soc. Med. (Sect. Urol.)* 15: 52-54 (Aug.) 1922.
- Eggers, H.: *Ztschr. f. urol. Chir.* 9: 427-432, 1922.
- Papin, Edmond: *Assoc. franç. d'urolog., Proc. Verh.* 22: 557, 1922.
- Mintz: *Khír. Arkh. Veliaminova* 29: 1047, 1923, cited by Papin, 598, 1935.
- Edmond: *Arch. d. mal. d. reins* 2: 24, 1925.
- Judd, E. S.; Braasch, W. F., and Scholl, A. J.: *Horseshoe Kidney*, J. A. M. A. 79: 1189-1196 (Oct. 7) 1922.
- Lynch, K. D., and Thompson, R. F.: *Urol. & Cutan. Rev.* 38: 239-242 (April) 1934.
- Chwalla, R.: *Arch. f. klin. Chir.* 183: 590-598, 1935.
- Baker, W. W., and Colston, J. A. C.: *J. Urol.* 35: 264-288 (March) 1936.
- Strode, J. E., *ibid.* 41: 285-293 (March) 1939.

stated to be excellent eight years, ten years and fourteen years after operation. In the remaining three cases only the immediate result is stated but this was excellent in all. These six cases reported since 1930 appear as cases 14 to 19 inclusive in table 1.

My six cases of horseshoe kidney and one case of unilateral fused kidney corrected by symphysiotomy and nephropexy on one or both sides, together with the nineteen cases reported in the literature, make a total of twenty-six cases for use in appraising division of the isthmus and nephropexy in cases of fusion anomaly.

My six personal cases are reported in summary and illustrated as follows:

REPORT OF CASES

CASE 1.—This case, from the urologic service of the Ancker Hospital, was originally reported in 1932 by my associate in the service, Philip F. Donohue.⁶

A woman aged 32 had had pain in the right lower quadrant of the abdomen for twelve years. A mass to represent the isthmus was not palpable. Pyelograms (fig. 1A) had the typical features of horseshoe kidney: low position, long axis oblique toward the midline below and medial direction of the inferior calices. There was slight dilatation of the pelves.



Fig. 4 (case 4).—A, preoperative urinary tract roentgenogram (left half; opaque catheter in ureter); B, preoperative right and left pyelo-ureterograms; C, postoperative left pyelo-ureterogram.

In March 1930, through a right flank incision, extraperitoneal exposure of the right half of the horseshoe kidney was made. The isthmus was divided and a right nephropexy was done. The operation gave complete and permanent relief of the right-sided pain.

Eight months after the operation the patient began to have pain on the left side exactly like the pain on the right side before operation. Left nephropexy was done, followed by complete and permanent relief of the left-sided pain. The pyelograms (fig. 1B) made long after the two operations showed completely normal pelves and disappearance of the pelvic dilatation.

Comparison of the before and after pyelograms (fig. 1) show beautifully the anatomic accomplishment of operation. This is accompanied by complete symptomatic relief. The dilatation originally present appeared to be insignificant but its disappearance the result of operation suggests that actually it was significant.

On June 1, 1940, more than ten years after operation, the patient reported continuing complete relief. There seemed to be no warrant to make another check-up pyelogram at that time.

CASE 2.—A woman aged 21 had had periodic bilateral back-ache and attacks of severe pain in the right flank and right lower quadrant of the abdomen for seven years. The right and left pyelograms (fig. 2a) showed the typical features of horseshoe kidney and slight pelvic dilatation.

Oct. 15, 1931, division of the isthmus and right nephropexy were made with immediate and permanent relief of the right-sided pain. During convalescence the patient began to have pain on the left side exactly like that on the right side before operation. Left nephropexy, December 8, was followed by complete and permanent relief of the left-sided pain.



Fig. 5 (case 5).—A, preoperative bilateral pyelo-ureterogram; B, postoperative right and left pyelo-ureterograms.

Two years after operation a bilateral pyelogram (fig. 2B) showed restoration to normal. Comparison of the before and after pyelograms (fig. 2) shows clearly what the operation accomplished.

On June 1, 1940, nine years after operation, the patient reported continuing complete relief. There seemed to be no warrant to make another check-up pyelogram at that time.

CASE 3.—A woman aged 25 had periodic pain in the right flank and right side of the abdomen for several years. Pyelograms (fig. 3A) showed the typical features of horseshoe kidney with slight dilatation of each pelvis. Resection of the isthmus and right nephropexy were done in July 1933, followed by complete and permanent relief of the right sided pain.

Within a year the patient began to have pain on the left side exactly like that present on the right side before operation. Left nephropexy in January 1935 was followed by complete and permanent relief of the left-sided pain.

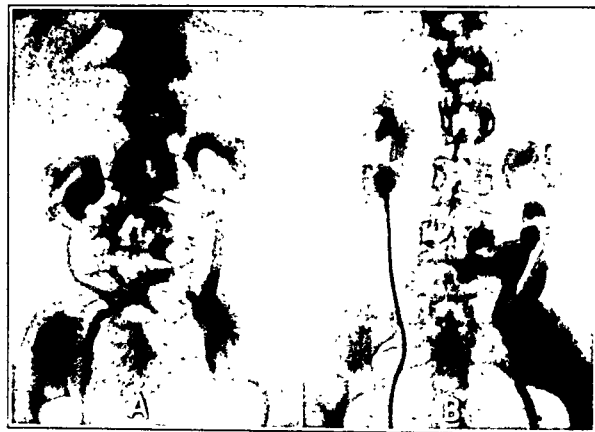


Fig. 6 (case 6).—A, preoperative bilateral pyelo-ureterogram; B, postoperative bilateral pyelo-ureterogram.

Excretion urograms (fig. 3B) made in April 1938, five years after the first operation, showed restoration to near normal. Comparison of the before and after pyelograms (fig. 3) shows well the anatomic accomplishment of the operation.

CASE 4.—This was the only case of failure. A man aged 38 had severe pain in the left flank, mild pain in the right flank and abdominal pain for several years. There was a stone in

the left kidney (fig. 4A) and with it bilateral hydronephrosis (fig. 4B) and deformity typical of horseshoe kidney. In June 1934 left pelviolithotomy, division of the isthmus and left nephropexy were done.

Later it was discovered the stone had been incompletely removed. Although the position of the kidney had been restored to near normal and the pelvic dilatation was slightly decreased (fig. 4C) the infection persisted and secondary nephrectomy was done eight months later.

CASE 5.—A woman aged 30 had had frequent severe pain in the right flank and right side of the abdomen for five years and occasional mild pain in the left flank and left side of the abdomen. The bilateral pyelogram (fig. 5A) showed the typical features of horseshoe kidney and bilateral hydronephrosis. In September 1934 division of the isthmus and right nephropexy were performed followed by gradual but finally complete relief of pain on the right side.

A year or so later the originally mild pain in the left flank and abdomen greatly increased. Left nephropexy in July 1938 was followed by complete and permanent relief. Relief of subjective symptoms has been complete and permanent. The most recent check-up pyelogram (fig. 5B) was made June 5, 1940, five and one-half years after the first operation and two years

right lower quadrant of the abdomen. The pyelogram (fig. 7A) showed the typical features of unilateral fused kidney with crossed ectopia of the left and lower segment.

For relief of the left-sided pain, two operations were contemplated. The pain appeared to have its origin in the left half of the fused kidney. Preliminary to any surgical attack on the "crossed-ectopic" left half of the fused kidney it seemed wise first to divide the isthmus and fix in normal position the separated right kidney. With the right half of the fused kidney thus restored to normal position and normal function, it would then be possible safely to perform a left nephrectomy if later operation on the left side disclosed vascular attachments or other technical difficulties making impossible a conservative procedure.

In June 1937, through a right flank incision with extra-peritoneal approach to the kidney, division of the isthmus and right nephropexy were done. Through this incision it was possible to displace the separated left kidney across the midline, though restoration of the left kidney to a completely normal position of course was not possible with this exposure.

The result to date, three years after operation, is excellent, there being complete relief of the left-sided pain complained of before operation. Since operation the patient has gone through an uneventful pregnancy terminated by normal delivery. In view of all this, no indication is found for doing the contemplated second operation on the left side.

The most recent check-up pyelogram (fig. 7B) was made June 5, 1940, three years after operation. It gives very poor outlining of the lower or left pelvis but sufficient to show that its position is somewhat improved. The right pelvis is well up in normal position. A comparison of this with the pyelogram made before operation shows what was accomplished (fig. 7).

COMMENT

In all of these cases a lumbar incision and extra-peritoneal approach to the kidney were employed. In all cases excellent exposure was secured: the procedure was carried out with facility and no formidable difficulty was encountered. In all cases relatively smooth convalescence followed the surgical procedure, and there was no mortality.

Items of interest in the occurrence and management of these cases are the following:

Six of the seven patients were women, all of whom were in the second or third decade. One patient was a man aged 38.

In all cases the chief complaint was pain and in most instances its character was fairly typical of renal origin. In all the cases obstruction and varying degrees of pelvic dilatation were demonstrated and in some there were varying degrees of upper tract infection and pyuria. In two of the cases the degree of pelvic dilatation amounted to outspoken hydronephrosis and one of these was complicated by stone.

In all cases operation was undertaken with relief of pain its chief objective. In all save one case (case 4) this object has been fully attained, with complete relief of painful symptoms. The one case of failure was due to faulty management, failure to remove a stone completely.

It should be noted that, in three cases (1, 2 and 3) of unilateral pain, division of the isthmus and relief of pain on the side of operation was followed in different periods by development of identical pain on the opposite side and that in these three cases correction of the abnormal position of the opposite half of the horseshoe kidney gave complete relief of the newly developed pain on the opposite side. In another case (case 5) originally mild pain on the opposite side gradually increased and a year and a half after the first operation was com-

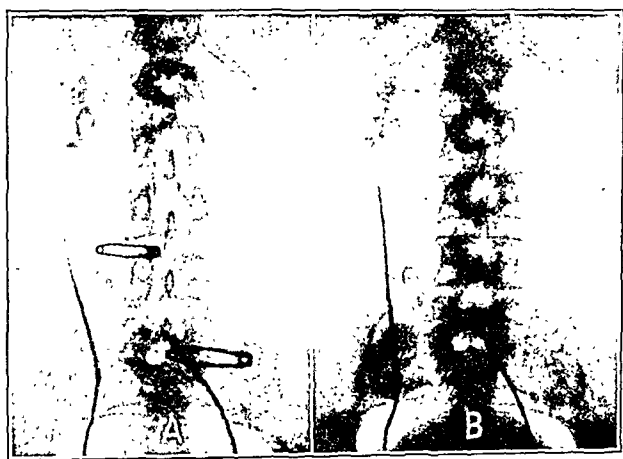


Fig. 7 (case 7).—A, preoperative bilateral pyelo-ureterogram; B, postoperative bilateral pyelo-ureterogram.

after the second operation. A comparison of this with the original pyelogram (fig. 5) shows what was accomplished by the operation.

CASE 6.—A girl aged 19 years at first had attacks of severe pain in the right lower quadrant of the abdomen. Later there was constant bilateral lumbar pain. The pyelogram (fig. 6A) showed the typical deformity of horseshoe kidney and grade 1 dilatation of each pelvis. On the left side there was duplication of the pelvis and upper ureter.

In July 1937 division of the isthmus and right nephropexy were performed. Following operation there were two attacks of acute pyelonephritis. Apart from these there has been complete and permanent relief of the right lower quadrant pain and of bilateral lumbar pain. The most recent check-up pyelogram (fig. 6B) was made June 6, 1940, three years after operation. It showed normal position of the right pelvis but no decrease of dilatation and no change in position of the left pelvis.

A comparison of this recent pyelogram with the original preoperative pyelogram (fig. 6) shows what was accomplished by operation.

CASE 7.—This was a case of unilateral fused kidney and was originally reported in the February 1930 issue of *International Abstracts of Surgery*.⁷

A girl aged 18 complained of left-sided abdominal pain for three years, at times very severe. A mass was palpable in the

7. Foley, F. E. B., and Wilmer, H. A.: *Internat. Abstr. Surg.* 70: 155-170, 1940, in *Surg., Gynec. & Obst.*, February 1940.

pletely relieved by nephropexy on the second side. In one case of bilateral pain (case 6) division of the isthmus and nephropexy on only one side gave relief of pain on both sides. In one case of unilateral fused kidney (case 7) left-sided pain was relieved by symphysiotomy and right nephropexy.

These seven cases make by far the largest individual experience thus far reported—in fact they represent almost a third of the total experience. In all save one case the eventual end result has been excellent ten years after operation in the earliest case, three years after operation in the most recent case.

The reports in the literature state the eventual end result in only three cases: excellent fourteen years, ten years and eight years after operation. In the case of Judd, Braasch and Scholl the result was excellent eighteen years after operation. In the remaining fifteen cases reported in the literature only the immediate result up to a few months after operation is stated, but in all it was excellent.

My own experience indicates that an immediately favorable result will prove to be a permanently favorable result if the case is followed long enough to bring the proof. At least among my seven cases there was only

TABLE 2.—*Results of Symphysiotomy With or Without Nephropexy*

Cases reported in literature.....	19
Cases, personal	7
Cases, total	26
Postoperative deaths	1 3½%
Poor results	1 3½%
Excellent or good results—early.....	14 54%
Excellent or good results—permanent.....	10 38%
Excellent or good results—total.....	24 92%
	26

one eventual poor result (case 4) and this was due to mismanagement—the failure to remove a calculus completely. This personal experience, indicating that an immediately favorable result will be permanent, increases the significance of the early favorable results reported in the literature.

SUMMARY AND CONCLUSIONS

The eighteen cases reported in the literature, the case of Judd, Braasch and Scholl followed by personal communication and my seven cases here reported are summarized in table 2 and the results may be stated as follows:

There was a total of twenty-six cases.

There was one postoperative death.

There was one poor result, which was due to mismanagement.

There were twenty-four good results. Of these, fourteen were reported as early results and ten were reported as permanent results.

The material presented warrants the conclusions that:

1. The anomaly horseshoe kidney not accompanied by any significant pathologic change may be productive of painful and other symptoms.

2. The symptoms caused by the anomaly horseshoe kidney can be relieved and normal anatomic relations can be restored by division of the renal isthmus and nephropexy on one or both sides.

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ACUTE ASCENDING PARALYSIS

CLINICAL AND PATHOLOGIC REPORT ON CASES WITH FATAL TERMINATION

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In 1859 Octave Landry¹ described a case of acute ascending paralysis in which there were no changes in sensation, muscular atrophy or disturbances of the sphincters, and no abnormalities were observed in the postmortem examination. Cases of ascending paralysis in which the clinical course resembled the one described by Landry have been called Landry's paralysis by many observers, and a definite clinical syndrome has been described. A previously healthy individual, after suffering from mild prodromal symptoms such as malaise, paresthesias in the lower extremities, anorexia, constipation and occasionally slight fever, develops a sudden flaccid paralysis of the lower extremities which rapidly ascends, involving next the abdominal muscles, the intercostals, the upper extremities and in fatal cases the muscles supplied by the bulbar nerves. Cases of descending paralysis have also been described, but these occur less frequently. The process may result in death within a few days or weeks, or if improvement does take place there may be complete recovery, the function returning first in the muscles last affected.

An infectious or toxic etiology has usually been ascribed to the condition, and enlargement of the spleen, hyperplasia of the lymph nodes, albuminuria and nephritis have been observed in some cases.² Among the infectious diseases that have been complicated by an ascending paralysis are syphilis, tuberculosis, diphtheria, influenza, typhoid, measles, mumps, malaria, pertussis, encephalitis, rabies, Rocky Mountain fever, smallpox, vaccinia, pneumonia, anthrax, varicella, gonorrhea and herpes. Rabies vaccine, diphtheria and tetanus antitoxin, alcohol, lead, arsenic and hematophyria have been reported as toxic etiologies. In a few instances organisms have been isolated from the cerebrospinal fluid or the spinal cord,³ but bacteriologic studies have given no consistent or conclusive results. A recent translator of Landry's original description and other authors believe that vitamin deficiency should be considered as an important etiologic factor,⁴ but this hypothesis remains to be proved. The term Landry's paralysis has also been erroneously applied to cases of poliomyelitis, transverse myelitis, myelomalacia⁵ and other varieties of myelitis of known etiology characterized by an ascending type of paralysis, but these conditions should obviously be differentiated from the true Landry type.

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Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Landry, Octave: Note sur la paralysie ascendante aiguë, *Gaz. hebdom. de méd.* 6: 472 (July 9), 486 (Aug. 5) 1859.

2. Wechsler, J. S.: A Textbook of Clinical Neurology, ed. 3, Philadelphia, W. B. Saunders Company, 1935, p. 125.

3. Boinet: Un cas de paralysie de Landry, *Gaz. d. hôp.* 72: 458 (May 2) 1899. Bradford, J. R.; Bashford, E. F., and Wilson, J. A.: Acute Infective Polynucleuritis, *Quart. J. Med.* 12: 88 (Oct.) 1918. Courmont, P.: Syndrome de Landry par lésions exclusives des cornes antérieures, *Arch. de neurol.* 8: 353 (Nov.) 1899. Leschke, E.: Ueber der Erreger der Landry'schen Paralyse, *Berl. klin. Wchnschr.* 51: 783 (April 27) 1914.

4. Brown, M. R.: Etiologic Study of Landry's Original Case of Acute Ascending Paralysis, *Arch. Neurol. & Psychiat.* 40: 809 (Oct.) 1938. Shattuck, G. C.: "Landry's Paralysis" in Relation to Vitamin B Deficiency, *Internat. Clin.* 1: 25 (Sept.) 1938.

5. Low, A. A.: Acute Ascending Myelomalacia, *Arch. Neurol. & Psychiat.* 21: 594 (March) 1929.

The pathologic observations in cases classified as Landry's paralysis have been varied and inconsistent. The earlier writers believed that pathologic changes were absent; this opinion may have arisen as the result of the lack of technical facilities at the time, although cases are still being reported in which no lesions are found. Oppenheim⁶ stated that the postmortem appearances were indefinite and contradictory; in many cases the examination was negative, in some there were disseminated foci of inflammation and exudation with capillary hemorrhages and swelling of the axis cylinders, and others showed inflammation of the anterior horns or a combination of a neuritis and a myelitis. He felt that in most cases the conditions resembled those seen in polyneuritis without being identical with it. Cadwalader⁷ described hyperemia and edema of the gray matter of the spinal cord with varying changes in the anterior horn cells but stated that there appears to be no certain method of determining whether the disease process originates in the nerve fibers, in the spinal cord, or in both. At the present, however, most authors agree that purely degenerative changes take place either in the anterior horn cells or in the peripheral nerves, but there are no evidences of inflammation or infiltration, no glial proliferation, and no degenerative changes in the white matter of the spinal cord.⁸

Many authors have questioned the use of the term Landry's paralysis and the consideration of the condition as a nosologic entity.⁹ As early as 1891 Eichberg stated that the name was unscientific and should be dropped. Much misunderstanding has resulted, however, from the fact that many dissimilar conditions have been classified as Landry's paralysis. Eichberg's own case obviously did not belong to the Landry group, as it showed an acute inflammatory reaction in the anterior horn cells, the perivascular spaces and the meninges. Other authors have added to the confusion by using the term Landry's paralysis for cases of poliomyelitis and polyneuritis in which the paralysis was of an ascending nature. Grinker,¹⁰ for example, states that poliomyelitis is the most common cause of Landry's paralysis and that diphtheritic polyneuritis is the next in frequency. Cobb and Coggeshall¹¹ say that most cases diagnosed as Landry's paralysis are fulminating examples of ordinary infantile paralysis. According to Osler¹² the differentiation between multiple neuritis and Landry's paralysis is often difficult, and it may be impossible in cases with sensory changes. Taylor and McDonald¹³ considered ascending paralysis as a transitional form

between conditions in which the pathologic changes are predominantly in the spinal cord and a complicated group of polyneuritides. Collier¹⁴ believes that the separation of Landry's paralysis and polyneuritis is artificial and that Landry's paralysis is a polyneuritis with associated spinal cord involvement; he¹⁵ even went so far as to say, in his Morrison Lectures before the Royal College of Physicians of Edinburgh in 1932, that Landry's paralysis is one of the most characteristic of all forms of peripheral neuritis—a destruction of function, rapidly advancing, spreading by tissue continuity, without discoverable histologic changes and, when not fatal, rapidly and completely recovering, and that every grade of transitional form between the rapidly spreading Landry's paralysis and the slowly advancing types of peripheral neuritis may be encountered.

Attempts at classification and differentiation of the various types of ascending paralysis have been of some value in understanding the group as a whole but have not entirely clarified the subject. Some authors¹⁶ have differentiated the poliomyelitic and polyneuritic varieties from those showing little or no pathologic change. Pette and Környey¹⁷ separated cases with purely degenerative changes, apparently on a toxic basis, from those showing outspoken signs of inflammation. They subdivided instances of Landry's paralysis showing inflammatory changes into those in which the evidences of inflammation were predominantly central, or cases of atypical poliomyelitis, and those in which the pathologic changes were predominantly peripheral. Two instances of the latter group were described by them and classified as cases of Landry's paralysis, but both showed sensory changes and loss of sphincter control, thus making the clinical diagnosis doubtful, and in addition the postmortem examination revealed lymphocytic and plasma cell infiltrations in the ganglions, the nerve roots and the meninges. Juba¹⁸ described a similar case in which there were degenerative changes associated with infiltrations in the spinal ganglions, but he spoke of this as a polyneuroganglioradiculitis, which is obviously a better term.

Certain authors believe, however, with Gordinier¹⁹ that ascending paralysis is a specific type of myelitis of unknown etiology which can be differentiated, both clinically and pathologically, from poliomyelitis and polyneuritis, even in complicated cases. The former can, as a rule, be excluded by its epidemiologic features, clinical signs, characteristic cerebrospinal fluid changes and definite patho-anatomic picture. In polyneuritis there is simultaneous involvement of both sensory and motor nerves, the process being manifest in various portions of the body but failing to follow the distribution usually seen in acute ascending paralysis. Even

6. Oppenheim, Hermann: *Lehrbuch der Nervenkrankheiten*, ed. 7. Berlin, S. Karger, 1923, pp. 832-840.

7. Cadwalader, W. B.: *Diseases of the Spinal Cord*, Baltimore, Williams & Wilkins Company, 1932, p. 139-142.

8. Büttner, W.: Zur Klinik, pathologischen Anatomie und Nosologie der aufsteigenden Lähmung (sogen. Landry'schen Paralyse), *Monatsschr. f. Psychiat. u. Neurol.* 75: 279 (April) 1930. Courville, C. B.: Pathology of the Nervous System, Mountain View, Calif., Pacific Press Publishing Association, 1937, p. 179. Freeman, Walter: Neuropathology, Philadelphia, W. B. Saunders Company, 1933, p. 168. Gartner, W.: Polyneuro-Radiculitis ascendens (Landry'schen Symptomenkomplex), *Deutsche Ztschr. f. Nervenheilk.* 123: 18, 1931. Pawljutschenko, E. M.: Zur Klinik und pathologischen Anatomie der "akuten aufsteigenden Landry'schen Paralyse," *Arch. f. Psychiat.* 89: 570, 1930. Collier.¹⁴

9. Eichberg, J.: A Case of Acute Ascending Paralysis—Rapidly Fatal Issue, *M. Rec.* 39: 226 (Feb. 21) 1891. Taylor, E. W., and Clark, J. E.: Landry's Paralysis: Remarks on Classification, *J. Nerv. & Ment. Dis.* 27: 177 (April) 1900.

10. Grinker Roy R.: *Neurology*, Springfield, Ill., and Baltimore, Charles C. Thomas, 1934, p. 221.

11. Cobb, Stanley, and Coggeshall, H. C.: Neuritis, *J. A. M. A.* 103: 1608 (Nov. 24) 1934.

12. Osler, William: *The Principles and Practice of Medicine*, New York, D. Appleton & Co., 1892, p. 836.

13. Taylor, E. W., and McDonald, C. A.: The Syndrome of Polyneuritis with Facial Diplegia, *Tr. Am. Neurol. A.* 57: 210, 1931.

14. Collier, James: Landry's Paralysis, in Christian, H. A.: *Oxford Medicine*, New York, Oxford University Press, 1936, vol. 6, pt. 1, p. 419.

15. Collier, James: Peripheral Neuritis, *Edinburgh M. J.* 39: 601 (Oct.) 1932.

16. Marie, P., and Tretiakoff, C.: Etude anatomo-pathologique de trois cas de maladie de Landry a forme medullaire, *Rev. neurol.* 37: 777 (July-Aug.) 1921. Goldby, Frank: Landry's Paralysis: A Clinical and Pathological Study, *J. Neurol. & Psychopath.* 11: 1 (July) 1930. Callewaert, P.: Deux observations anatomocliniques de maladie de Landry, *J. belge de neurol. et de psychiat.* 36: 368 (June) 1936.

17. Pette, H., and Környey, S.: Zur Histologie und Pathogenese der akutentzündlichen Formen der Landry'schen Paralyse, *Ztschr. f. d. ges. Neurol. u. Psychiat.* 128: 390, 1930.

18. Juba, A.: Ueber einen perakut verlaufenen Fall von Polyneuroganglioradiculitis ascendens, *Deutsche Ztschr. f. Nervenheilk.* 142: 265, 1937.

19. Gordinier, H. C.: Poliomyelitis versus Landry's Paralysis, *Ann. Int. Med.* 3: 892 (March) 1930.

in conditions such as "infectious neuronitis" (Foster Kennedy; Gilpin, Moersch and Kernohan,²⁰ and others) and in the cases of ascending paralysis in troops described by Casamajor,²¹ a clinical and pathologic differentiation can usually be reached. The same is true of the cases of polyneuritis with albuminocytologic dissociation described by Guillain and Barré.²²

In an effort to evaluate these varying points of view and to come to some conclusions as to the justification of the use of the terms ascending paralysis or Landry's paralysis, some cases that have recently been studied both clinically and pathologically in the University Hospital have been reviewed.

REPORT OF CASES

CASE 1.—M. K., a painter aged 65, had noticed shooting pains in the feet for several months. Three weeks before admission he had diarrhea and a slight head cold and two weeks later had suddenly become nauseated, vomited, and noted cramping pains in the lower part of the abdomen. Following this he had weakness and later an ascending paralysis, first involving the feet, then the thighs, trunk and upper extremities. There was tingling of the hands and feet but no definite loss of sensation, and there was no disturbance of bowel or bladder control. Two days before admission he developed hoarseness, dysphagia, and weakness of the neck muscles, and shortly after this difficulty in breathing.

On admission the patient was dyspneic and cyanotic. Respirations were intercostal in type. Speech was reduced to a whisper and swallowing was difficult. There was limitation of lateral rotation of the eyeballs to each side; the ocular fundi were normal, as was the reaction of the pupils. There was weakness of the muscles of facial expression on both sides, and

trapezius muscles. The patient was unable to move his extremities. The tendon and abdominal reflexes were absent. There was no response following plantar stimulation. The sensory examination was unsatisfactory but no definite disturbance in sensation was elicited.

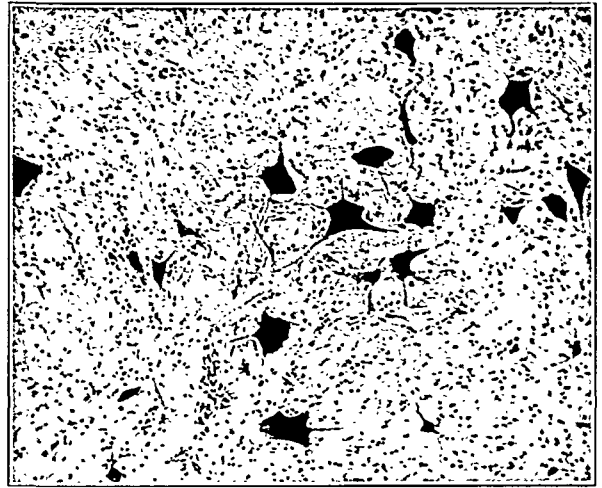


Fig. 2 (case 1).—Section of anterior horn cells showing shrinkage and pyknosis. Nissl stain; Zeiss objective 40 \times ; ocular F 2.

Because of the marked difficulty in breathing the patient was placed in a respirator on admission to the hospital, and as a result further examinations including those of the cerebrospinal fluid could not be carried out. There was a gradual failure of respiration and circulation, and death occurred in forty-eight hours.

The postmortem examination revealed an acute purulent bronchitis and bronchopneumonia with atelectasis, emphysema and pulmonary congestion. The brain and spinal cord were edematous and hyperemic and the meninges were congested. There were many small hemorrhages into the meninges and the gray matter of the cord. The predominant microscopic pathologic changes were noted in the nerve roots and the spinal ganglions. There were large deposits of lipoids in the periphery of the neurons and within the nerve fibers, as demonstrated both by scarlet red and by osmic acid stains (fig. 1). The structure of the ganglions and nerve fibers was otherwise unchanged, the myelin was not appreciably broken down, and there was no evidence of inflammation. Nissl stains of the spinal cord showed shrinkage, pyknosis and varying degrees of chromatolysis of the anterior horn cells (fig. 2), and scarlet red and osmic acid stains showed lipoids within the neurons. There were many small hemorrhagic areas in the gray matter, some of which were surrounded by minute areas of necrosis. There were no evidences of infiltration, inflammation or exudation in the nerves or the spinal cord, and there was no destruction of the myelin sheaths. No definite pathologic changes were demonstrable in the nuclear area of the pons or medulla.

CASE 2.—Mrs. B. S., a white woman aged 48 whose past medical history was without significance, had been well until two weeks before admission to the hospital, at which time she had an attack of respiratory difficulty diagnosed as asthma and relieved by oral and hypodermic medication. One week later she noticed heaviness and progressive weakness of the feet, which ascended to involve the legs and later the arms and hands. There were paresthesias in the hands and feet, but there was no definite loss of sensation.

At the time of admission the patient was dyspneic and moderately cyanotic. Moist rales were heard throughout the lungs and there was an area of dullness at the base of the left lung. There was no disturbance of superficial sensation or of sense of position; vibratory sense was slightly diminished at the ankles, but deep pain sense was increased in the calf muscles and achilles tendons. The pupils reacted normally to light and in accommodation. The extra-ocular movements were

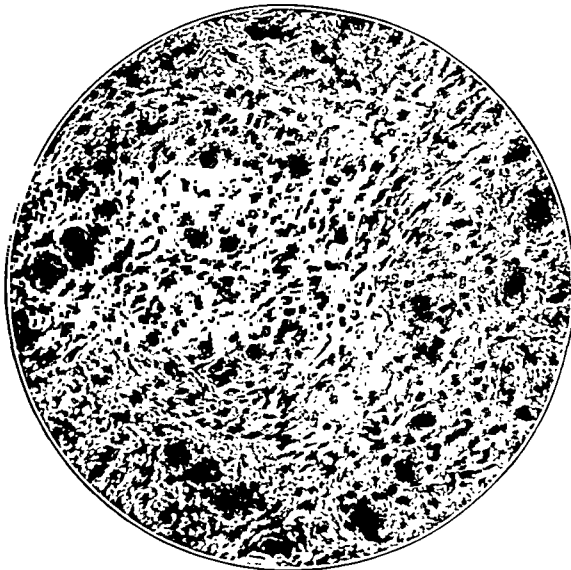


Fig. 1 (case 1).—Section of deposits of lipoids in the periphery of the neurons of the spinal ganglions and within the nerve fibers. Scarlet red stain; Zeiss objective 40 \times ; ocular F 2.

the soft palate could not be elevated. The tongue could not be protruded beyond the lips, but there was no atrophy or tremor. There was bilateral weakness of the sternocleidomastoid and

20. Kennedy, Foster: Infective Neuronitis, *Arch. Neurol. & Psychiat.* 2: 621 (Dec.) 1919. Gilpin, S. F.; Moersch, F. P., and Kernohan, J. W.: Polyneuritis. A Clinical and Pathologic Study of a Special Group of Cases Frequently Referred to as Instances of Neuronitis, *Arch. Neurol. & Psychiat.* 35: 937 (May) 1936.

21. Casamajor, Louis: Acute Ascending Paralysis among Troops, *Arch. Neurol. & Psychiat.* 2: 605 (Dec.) 1919.

22. Guillain, G.; Barré, J. A., and Strohl, A.: Sur un syndrome de radiculo-nevrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire, *Bull. et mém. Soc. méd. d. hôp. de Paris* 40: 1462 (Oct. 13) 1916.

normal. There was a slight but definite weakness of the muscles supplied by the left facial nerve. Articulation was normal. The sternocleidomastoid and trapezius muscles contracted normally and the tongue protruded in the midline. Aside from shrugging of the shoulders the patient was unable to carry out any movement of the upper or lower extremities. There was no atrophy, and no fibrillations were seen. All tendon and cutaneous reflexes were absent. There were no pyramidal tract signs. The urinalysis, blood count, and blood Kahn test gave negative results. The spinal fluid pressure was 150 mm. of water, with no block, and the fluid contained one lymphocyte per cubic millimeter; the Pandy and Nonne-Apelt tests were strongly positive, the total protein content was 111 mg. per hundred cubic centimeters, the Kahn reaction was negative, the colloidal gold curve was 0011100000, and the mastic curve was 122100. Examination of the urine, hair and nails for lead and arsenic was carried out with negative results.

The paralysis of the extremities continued unabated, and two days after admission the patient noted difficulty in swallowing and talking with progressive respiratory distress. Pneumonia developed and death occurred two weeks after admission.

The postmortem examination showed bronchopneumonia in the lower lobe of the left lung and atelectasis in the lower lobe of the right. Gross examination of the brain revealed pronounced hyperemia. In the spinal cord the predominant congestion was in the anterior horns, the cells of which showed marked swelling with displacement of the nuclei. The tigroid substance was broken down; in some cells it was evenly distributed throughout and dustlike in appearance, while other cells stained a deep pinkish blue with thionin and showed no details. Many of the swollen cells contained large vacuoles, and some with three or more exhibited a honeycombed appearance (fig. 3). Scarlet red and Marchi stains showed accumulations of lipoids within the neurons. The vessels of the cord were congested and engorged but there was no evidence of infiltration or exudation and no degeneration of the myelin sheaths. The motor nuclei within the medulla showed changes similar to those present in the anterior horn cells. There was no inflammatory reaction in the ganglions and no definite evidence of any pathologic process in the peripheral nerves.

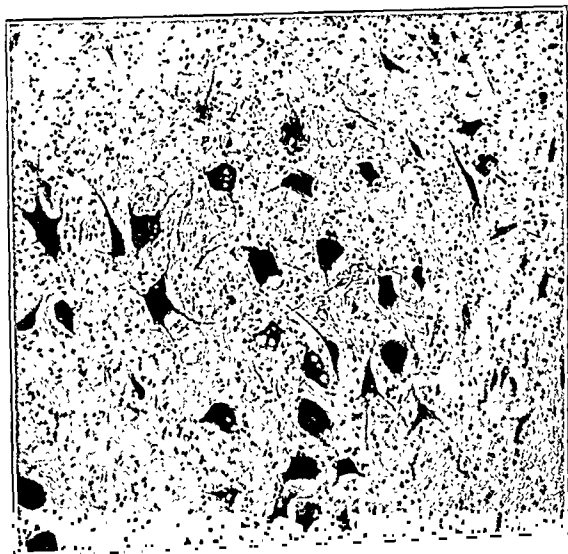


Fig. 3 (case 2).—Section of anterior horn region showing swelling and vacuolization of neurons. Nissl stain; Zeiss objective 40 \times ; ocular F 2.

CASE 3.—M. P., a girl aged 18 months, developed what appeared to be pain in the legs and later in the arms, followed by a complete paralysis of the lower and a partial paralysis of the upper extremities. There was a brief elevation of temperature at the time of the onset of the symptoms. Six weeks later respiratory difficulty appeared and the temperature again became elevated.

At the time of admission to the hospital the patient was dyspneic and cyanotic. The respirations were 30 per minute,

the pulse rate was 130 and the rectal temperature was 101 F. There was dulness with bronchial breathing over the base of both lungs. The pupils reacted normally and there was no apparent difficulty in talking or swallowing. There was a flaccid paralysis of the upper and lower extremities. The triceps reflexes were diminished, and the biceps, patellar and achilles reflexes were absent. The abdominal reflexes were

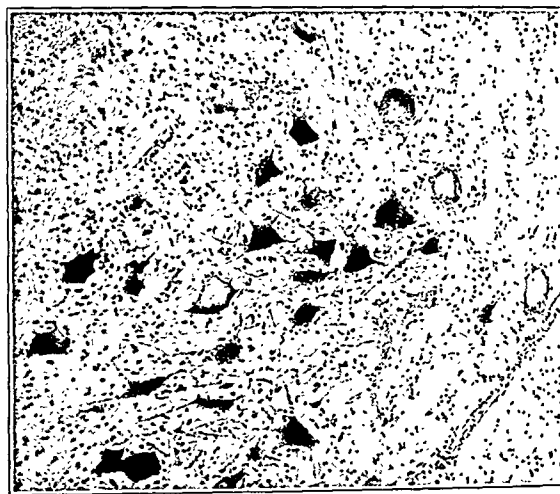


Fig. 4 (case 3).—Section of anterior horn region showing outspoken primary irritation of the neurons with chromatolysis and swelling. Nissl stain; Zeiss objective 40 \times ; ocular F 2.

not obtained. There was no Babinski sign. Superficial and deep pain sensations were apparently normal. There was no demonstrable muscle tenderness and there were no signs of meningeal irritation. The urinalysis and the Kahn tests on the blood gave negative results. Blood count showed 13,050 leukocytes per cubic millimeter, 79 per cent of which were polymorphonuclear cells. A spinal puncture was not performed.

The child was placed in an oxygen tent but her respiratory difficulty increased and she became unable to swallow. Death occurred twenty-four hours after admission.

The postmortem examination showed a severe bilateral, confluent, purulent, lobular pneumonia. There were moderate congestion and edema of the brain, meninges and spinal cord but no other gross pathologic abnormalities. Microscopic examination showed pronounced changes in the anterior-horn cells, especially in the lumbar and sacral segments. The cells were greatly swollen and many were vacuolated. The tigroid substance was disintegrated and broken down into fine dustlike particles which stained a pinkish blue with thionin. The nuclei were either shrunk and pushed to the periphery of the cells or were completely destroyed (fig. 4). In other segments, especially those of the thoracic cord, there were fewer swollen cells but many which stained a deep blue so that few details could be made out, and some which were reduced to indistinctly outlined bodies filled with disintegrated tigroid material. In certain sections the neurons in the anterior horns were greatly reduced in number and those which remained were small and shrunk. There were no signs of inflammation or glial proliferation and there was no degeneration of myelin. The peripheral nerves were normal. There were no demonstrable changes in the medulla.

CONCLUSIONS

These are instances of acute ascending paralysis of unknown etiology. The pathologic changes were not identical, but in all there were evidences of a degenerative process involving the motor nuclei or the peripheral nerves or both. There were no signs of inflammation, such as cellular infiltration or glial proliferation, and no degenerative changes in the white matter of the spinal cord. The predominant gross pathologic finding was hyperemia of the anterior horn region. The outstanding microscopic change, the degen-

eration of the neurons, assumed different forms. In case 1 it consisted of shrinkage and pyknosis, which may be considered as a primary phenomenon, but it was accompanied by degenerative changes in the nerve roots and the spinal ganglions. In case 2 there were swelling, chromatolysis, displacement and fragmentation of the nuclei, and vacuolization, which is assumed to indicate an axonal type of degeneration secondary to changes in the axis cylinders. Case 3 showed a pronounced axonal reaction in some segments with pyknosis and reduction in the number of the neurons in others. It can be assumed from these observations that the degenerative process is one that involves either the motor nuclei or the peripheral nerves or both and is therefore characterized by involvement of part or all of the final common pathway of the motor impulses. In spite of some variability in the changes they were purely degenerative in all cases, and to a certain extent each showed some evidence of both pyknosis and swelling. It is entirely possible that the syndrome is a transitional form between certain types of polyradiculoneuritis (Guillain-Barré syndrome) and varieties of myelitis and encephalitis.

The etiology of the process cannot be arrived at from this study. As there are no signs of inflammation and the changes in the nervous system are essentially degenerative in nature, it can probably be assumed that we are dealing with an acute toxic process affecting both the central and the peripheral nervous system.²³ A filtrable virus etiology has been suggested, but this has not yet been proved.²⁴

Precedent has established the use of the terms Landry's paralysis and acute ascending paralysis. Diller²⁵ in 1902 stated: "The term Landry's paralysis cannot be dropped. It has been used too long to be erased from our nomenclature." If these terms are to be used, however, they should not be interpreted as signifying a definite nosologic entity due to a single etiology. The terms should be used only in those cases in which the clinical syndrome is similar to that described by Landry and no definite etiology such as poliomyelitis or some specific toxin or infection is suspected. When the foregoing terms are used they should be considered as descriptive of the mode of onset and progression of the condition² rather than as a final diagnosis. Cases in which the etiology is known but the syndrome closely resembles that seen in acute ascending paralysis may be spoken of as cases of Landry's syndrome.

23. Brussilowski, L.: Zur Lehre von der akuten aufsteigenden Landry'schen Paralyse, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **111**: 515, 1927.
Grunewald, E. A.: Studien zur Pathogenese der Landry'schen Paralyse, *J. f. Psychol. u. Neurol.* **29**: 403, 1923. Willis, F. E. S., and Jewell, J. W. F.: A Case of Landry's Paralysis of Descending Type, *Lancet* **1**: 132 (Jan. 18) 1930.

24. Demme, H.: Zur Pathogenese der entzündlichen Form der Landry'schen Paralyse, *Deutsche Ztschr. f. Nervenhe.* **125**: 1, 1932. Cobb and Coggeshall.¹³

25. Diller, Theodore: A Study of Landry's Paralysis, with a Report of Three Nonfatal Cases, *J. Nerv. & Ment. Dis.* **29**: 577 (Oct.) 1902.

Normal Food Requirements.—Gillett has suggested that the family food budget be divided into fifths: one fifth for vegetables and fruits, one fifth or more for milk and cheese, one fifth or less for meat, fish and eggs, one fifth or more for bread and cereals and one fifth or less for sugars, fats and other groceries and food adjuncts. Whatever the level of food expenditure, at least as much should be spent for milk (including cream and cheese) as for meats, poultry and fish, and as much should be spent for fruits and vegetables as for meat, poultry and fish.—Smilie, Wilson G.: *Public Health Administration in the United States*, New York, Macmillan Company, 1940.

POLYRADICULONEURITIS (GUILLAIN-BARRÉ SYNDROME)

FOLLOWING THE USE OF SULFANILAMIDE AND
FEVER THERAPY

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During recent years two valuable therapeutic agents, sulfanilamide and fever therapy, have been added to the armamentarium in the treatment of disease. However, like other therapeutic measures, they may be accompanied or followed by undesirable effects in a certain percentage of cases. It is often difficult to decide, when two therapeutic agents are used concomitantly or consecutively, which agent is responsible for the favorable effect on the disease or, in some instances, even the undesirable complication.

Numerous toxic manifestations have been described following the use of sulfanilamide and its derivatives. Reports indicating a toxic action of sulfanilamide on the peripheral nervous system are few. Ornsteen and Furst¹ reported a case of peripheral neuritis which followed the ingestion of 130 Gm. of sulfanilamide. Janet² observed one case of multiple neuritis of the arm and thorax which lasted only three days. Vaughn³ recently reported a case of neuritis of the left anterior tibial nerve occurring in a patient with gonorrhea during treatment with sulfanilamide. This was the only case which he observed in 650 cases in which intensive sulfanilamide therapy was administered. A case of optic neuritis was reported by Bucy.⁴ However, peripheral neuritis has been frequently reported following the use of disulfyl-sulfanilamide. Recently we have observed two cases of peripheral neuritis which developed in patients treated for staphylococcal infections with sulfamethylthiazole.

Certain evanescent symptoms referable to the nervous system may occur during fever treatment. In this clinic we have occasionally observed such symptoms as delirium, coma, convulsions, vomiting and localized muscular weakness. These symptoms have been attributed to dehydration, cerebral edema, anoxemia and in a few cases of syphilis probably actual vascular lesions in the central nervous system. These symptoms are found during or immediately following treatment.

During the past two years we have observed six cases in which a more extensive and rather definite, stereotyped syndrome developed from ten to sixteen days following fever treatments of fifteen hours at 41.5 C. (106.7 F.). Nothing similar had been noted following the treatment of approximately 1,100 fever cases since 1930, and the syndrome is so striking and temporarily disabling as to have been called to our attention before this, if it has occurred in our group of patients.

Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

From the Department of Medicine, Division of Neurology (Drs. Garvey and Jones) and the Department of Radiology (Dr. Warren) of the University of Rochester School of Medicine and Dentistry.

1. Ornsteen, A. M., and Furst, William: Peripheral Neuritis Due to Sulfanilamide, *J. A. M. A.* **111**: 2103-2104 (Dec. 3) 1938.

2. Janet, Jules: Protest Against Sale of Sulfanilamide over the Counter, *Paris letter*, *J. A. M. A.* **110**: 1501 (April 30) 1938.

3. Vaughn, J. R.: Peripheral Neuritis During Administration of Sulfanilamide, *Am. J. Syph., Gonorr. & Ven. Dis.* **23**: 745 (Nov.) 1939.

4. Bucy, Paul C.: Toxic Optic Neuritis Resulting from Sulfanilamide, *J. A. M. A.* **109**: 1097-1098 (Sept. 25) 1937.

The syndrome under discussion in many respects is similar to that described by Guillain, Barré and Strohl⁵ and is generally known as the Guillain-Barré syndrome. They describe it as a syndrome characterized by motor disturbances, loss of tendon jerks with preservation of cutaneous reflexes, paresthesias with slight disturbances of objective sensitivity, tenderness on pressure of the muscles, little changes in the electrical reaction of nerve or muscles, and noteworthy hyperalbuminosis of the cerebrospinal fluid in the absence of cytologic reaction (albuminocytologic dissociation).

REPORT OF CASES

CASE 1.—B. S., a girl aged 17 years, was admitted to the Rochester Municipal Hospital on June 20, 1938, because of lower abdominal pain and a vaginal discharge of three months' duration. A diagnosis of gonorrheal cervicitis was made at a local hospital and she received 38 Gm. of sulfanilamide between April 6 and April 10, 1938. Cervical cultures for *Neisseria gonorrhoeae* were positive following the course of sulfanilamide, and she was referred to this hospital for fever therapy.

The patient was well developed and well nourished. Vital signs were normal. The general physical examination was negative, except for some erosion of the cervix and a thick purulent vaginal discharge. Neurologic examination was negative.

Examination of the blood revealed 5,100,000 red blood cells, hemoglobin content 85 per cent, white cells 12,000. The Kahn and Wassermann tests were negative. The nonprotein nitrogen was 27 mg. per hundred cubic centimeters, icterus index 6, blood chlorides (under oil) 626 mg. per hundred cubic centimeters. Cervical cultures revealed *Neisseria gonorrhoeae* with a thermal death time of twenty hours at 41.5 C.

After the routine preparation for fever therapy on June 24 she was given fifteen hours of fever at 41.5 C. with a vaginal heater at 43.5 in situ for eight hours. She tolerated the procedure well except for postfever nausea and vomiting (chloride deprivation). On the second day following fever she became clinically icteric and had an icterus index of 20. On June 26 she was given an infusion of 1,000 cc. of 5 per cent dextrose solution into both thighs. Following this her recovery was uneventful. Three successive cervical cultures were negative prior to her discharge from the hospital on July 1.

The patient returned to the clinic on July 5 complaining of pain and soreness of both thighs. The temperature and pulse were normal. Both thighs were tender, swollen and indurated. A diagnosis of thrombophlebitis was made. The swelling and tenderness promptly subsided with rest in bed and she was discharged four days later.

On August 13 she was admitted to the hospital because of difficulty in walking. This symptom had been first noticed following her last discharge from the hospital on July 9. Associated with the disturbance of gait, which frequently caused her to fall, she had sharp shooting pains which radiated down both lower extremities. There was no history of sphincter or sensory disturbance.

On examination the cranial nerves were normal. Neurologic survey of the upper extremities was negative. The abdominal reflexes were present. The lower extremities were weak. She was able to walk unassisted, but the gait was waddling and unsteady. The calf muscles were flabby and one observer noted fibrillary tremors in the thigh muscles. The knee jerks were normal and the achilles reflexes diminished. There was no sensory disturbance. The plantar reflex was flexion on both sides. There were no abnormal physical manifestations.

A lumbar puncture on August 16 yielded a clear, colorless fluid under pressure of 190 mm. of water. The Queckenstedt test was negative. The fluid contained 4 cells per cubic millimeter. Total protein was 170 mg. per hundred cubic centimeters.

5. Guillain, Georges; Barré, J. A., and Strohl, A.: Sur un syndrome de radiculoneurite avec peralduminose du liquide céphalo-rachidien sans réaction cellulaire: Remarque sur les caractères cliniques et graphiques des réflexes tendineux, *Bull. et mém. Soc. méd. d. hôp. de Paris* 40: 1462 (Oct. 13) 1916.

The Wassermann reaction and gold curve were negative. On September 10 the spinal fluid was normal except for a total protein content of 140 mg. per hundred cubic centimeters. The spinal fluid at the time of the last puncture on November 21 was normal. The total protein content was 45 mg. per hundred cubic centimeters. The examination of the patient in December 1939 revealed no abnormalities.

CASE 2.—M. P., a man aged 34, was admitted to Strong Memorial Hospital on Nov. 8, 1938, because of a persistent urethral discharge. In 1936 the patient contracted an anterior urethritis, which gradually cleared up with local treatments given over a period of nine months. Two months before admission, one week following exposure, he again noted a profuse urethral discharge. During October he received 63 Gm. of sulfanilamide, 50 cc. of azosulfamide intramuscularly, and seven five hour fever treatments at another institution, without any decrease in the amount of the urethral discharge. He was then referred to this hospital for generalized hyperthermia.

The patient was well developed. The physical examination was negative except for the profuse urethral discharge. There were no abnormal neurologic symptoms or signs.

Examination of the blood revealed a moderate normocytic anemia. The hemoglobin was 10.8 Gm., red blood cells 3,090,000 per cubic millimeter, white blood cells 9,000. Blood chemistry was within normal limits. The Wassermann and Kahn tests on the blood were negative. The gonorrhea complement fixation test was plus-minus. Gonococci were cultured from the first specimen of voided urine. The thermal death time for the strain isolated was in excess of twenty-three hours at 41.5 C.

On November 11 he was given fifteen hours of fever therapy at 41.5 C. He tolerated the procedure well and without any postfever reaction or change in the blood chemistry. Three successive urethral cultures were negative for *Neisseria gonorrhoeae* and he was discharged on November 15.

The patient returned to the hospital on December 4 complaining of weakness and stiffness of the legs. These symptoms began twelve days after the hyperthermia. Associated with the weakness there were mild paresthesias of the legs and hyperhidrosis of the feet. He had no symptoms referable to the cranial nerves, upper extremities or sphincters. The general physical examination showed no abnormalities of the cranial nerves or upper extremities. There was weakness of both legs, particularly the flexors of the thighs and dorsiflexors of the feet. The gait was rather characteristic of that seen in progressive muscular dystrophy. He had difficulty in climbing stairs and he was unable to stand on his toes. The knee reflexes were present but diminished. The left achilles reflex was not definitely elicited and the right was greatly diminished. Tactile and thermal sensations were diminished over the feet and lower half of the legs. Vibration sensation was diminished over the malleoli but postural sensation of the toes was normal. There was excessive perspiration of the feet. The calf muscles were tender to palpation. A lumbar puncture yielded a clear, colorless spinal fluid under pressure of 110 mm. of water. The Queckenstedt test was normal. The fluid contained 4 cells per cubic millimeter and the total protein was 160 mg. per hundred cubic centimeters. Blood and spinal fluid Wassermann tests were negative. The colloidal gold curve was 0000121000. The patient was discharged from the hospital on December 6.

The patient returned to the hospital on December 22 and reported considerable improvement in gait and muscle power. The neurologic signs remained unchanged. A second lumbar puncture yielded a normal spinal fluid except for a total protein content of 110 mg. per hundred cubic centimeters. Further follow-up on this case was impossible, since the patient left the country at this time.

CASE 3.—F. S., a youth aged 18, was admitted to the Rochester Municipal Hospital on Feb. 11, 1939, because of sore throat, rash and a penile lesion. Six weeks before admission he was exposed to syphilis and two weeks following this exposure he developed a hard, painless, ulcerative lesion of the glans penis. The penile lesion began to heal after a period of about three weeks and at about this time he developed a macular eruption over the trunk and upper extremities. Three days before admission he developed a severe sore throat and pain in the

right ear. It was for relief of the latter symptoms that he sought medical aid. The past history was irrelevant.

On examination the patient was found to be in considerable discomfort, the result of the ear pain and sore throat. The temperature was 37.7 C. (99.8 F.) and the pulse 92. The pharynx was injected and edematous. There were bulging and redness of the right ear drum. A maculopapular eruption was present over the trunk and upper extremities. There was generalized shotty lymphadenopathy. A typical chancre in the process of healing was present on the glans penis. Examination of the heart, lungs and abdomen were negative.

Laboratory examination of the blood revealed 5,080,000 red blood cells per cubic millimeter and 8,100 white blood cells, with a normal differential count. The urine and stool examinations gave negative results. The blood Wassermann and Kahn tests were 4 plus. Dark field examinations of material obtained from the penile lesion revealed *Spirochaeta pallida*.

On February 14 the patient was given fifteen hours of fever therapy at 41.4 C., which he tolerated very well. Dark field examinations of scrapings from the penile lesion on February 15, 16, 17 and 20 were negative for *Spirochaeta pallida*. Chemotherapy was started on February 25 and the patient received one injection of arsphenamine, two injections of neoarsphenamine and three injections of mercuric succinimide before his discharge from the hospital on March 2. At the time of discharge his blood Wassermann test was 4 plus in 1:32 dilution. The primary and secondary manifestations of syphilis had completely disappeared.

He was given 0.4 Gm. of arsphenamine on March 4. One week later, when he returned for his next treatment, he complained of pain across the lower part of the back, cramps in his legs and difficulty in walking. The onset of these symptoms apparently occurred immediately after his discharge from the hospital on March 2. A lumbar puncture done on March 14 yielded a clear, colorless spinal fluid under normal pressure. There were no cells in the spinal fluid, but the total protein content was 160 mg. per hundred cubic centimeters. The Wassermann test reported on the spinal fluid was noncholesterinized antigen \pm , cholesterinized antigen 3+, Kahn test —. The colloidal gold test showed no abnormality.

The patient was referred to the Neurological Clinic on March 15. He complained of difficulty in walking, pains in the legs and excessive perspiration of the feet. These symptoms had developed seventeen days after the fever treatment. There were no symptoms referable to the cranial nerves, upper extremities or sphincters. The patient walked, unaided, with a waddling, steppage type of gait. There was marked weakness of the flexors and extensors of both feet. He was unable to elevate the heels more than an inch from the floor when attempting to stand on his toes. The pelvic girdles and thigh muscles showed some slight weakness. There was no localized atrophy or fibrillary tremors observed in the musculature of the lower extremities. The lower tendon reflexes were hyperactive and equal. The Babinski sign could not be elicited. Deep and superficial sensations were normal. There was marked hyperhidrosis of the feet.

The patient was seen in the Neurology Clinic one month later, on April 15. He reported considerable improvement in the strength of the lower extremities but he was still unable to walk long distances without fatigue. The gait showed considerable improvement and the muscular weakness was less marked than formerly. There was the same tenderness on palpation of the popliteal spaces and also on the lateral aspects of the legs over the peroneal nerves. The tendon reflexes were still hyperactive.

A lumbar puncture done on April 22 yielded a normal spinal fluid, except for total protein content of 120 mg. per hundred cubic centimeters. The spinal fluid Wassermann and Kahn tests were negative.

On May 20 the patient reported some improvement in the motor power of the lower extremities but the gait was still abnormal. He was seen again in December 1939, and at this time the gait was normal. Reexamination in April 1940 revealed no abnormalities. The total protein content of the spinal fluid was 35 mg. per hundred cubic centimeters.

CASE 4.—J. A., a man aged 24, was admitted to the Rochester Municipal Hospital on April 14, 1939, with a diagnosis of chronic myelogenous leukemia. The disease began thirteen months before admission with hemorrhage from the gums following the extraction of several teeth. He had been treated with solution of potassium arsenite at intervals in an effort to keep the white blood cells below 1,000,000 per cubic millimeter. He complained of some numbness and tingling of the hands while taking this medication, but no muscular weakness had been noted.

On examination the patient appeared chronically ill. Vital signs were normal except for a temperature of 38.8 C. (101.8 F.). The skin showed some brownish pigmentation. There was marked enlargement of the spleen and liver. Blood studies showed a moderate normocytic hyperchromic anemia and the white blood cell count was 207,600 cells per cubic millimeter. The blood smear was typical of myeloid leukemia. The neurologic examination was negative except for loss of the achilles reflexes. The patient was given a course of high voltage roentgen therapy which resulted in decrease in the size of the spleen and reduction of the white blood cells to 75,000 per cubic millimeter. He was then discharged from the hospital on May 12 and was followed in the Blood Clinic.

On October 31 he complained of a penile lesion which had been present for about one month. Examination revealed two superficial lesions without induration of the glans penis. Dark field examination of material obtained from these lesions revealed numerous spirochetes. Blood Wassermann and Kahn tests taken at this time were negative. There were no secondary manifestations of syphilis.

The patient was readmitted to the hospital and after the routine preparation he was given fifteen hours of hyperthermia at 41.5 C. on November 6. The white blood cell count at the beginning of treatment was 119,000 and at the conclusion 120,000. No spirochetes could be found on dark field examination after five hours of fever. On November 9 the dark field examination was still negative for spirochetes. At the time of discharge, November 14, the penile lesion had healed, there were no secondary lesions and the blood Wassermann test was negative. The white blood cell count was 318,000 per cubic millimeter.

The patient returned to the clinic on November 22 complaining of sharp pains in his lower back and legs, weakness of the legs, difficulty in walking and numbness of his feet. These symptoms began eleven days following the fever treatment. The weakness of the legs was so marked that he could not climb stairs or walk on level ground without some assistance. There was no sphincter disturbance. The pains in his back and legs were increased by such acts as coughing, sneezing and straining. The abnormal neurologic signs were limited to the lower extremities. The lower tendon reflexes were absent. All muscle groups in the lower extremities were weak. He was unable to rise on his toes. His gait was waddling in type and very unsteady. The manner of arising from the recumbent position was similar to that observed in progressive muscular dystrophy. There was diminution of pain and temperature sensation over the lower third of the legs and feet, of patchy distribution. There were no pyramidal tract signs. Spinal fluid examination on November 22 was normal except for a total protein content of 79 mg. per hundred cubic centimeters. Subsequent lumbar punctures revealed total protein values as follows: December 3, 140 mg.; December 21, 130 mg.; April 26, 1940, 50 mg. At the time of his last examination, April 26, he was greatly improved although there was still some evidence of muscular weakness. The neurologic examination was negative except for absence of the achilles reflex.

CASE 5.—C. S., a woman aged 26, was admitted to Strong Memorial Hospital on Oct. 9, 1939, because of a vaginal discharge and lower abdominal pain. Four months before admission she acquired a gonococcal infection and since this time she had taken 500 Gm. or more of sulfanilamide without any improvement in her symptoms.

The patient was undernourished. Vital signs were normal. The physical examination was negative except for tenderness in both lower quadrants and erosion of the cervix and the vaginal discharge. The neurologic examination was negative.

Examination of the blood revealed 4,400,000 red blood cells, hemoglobin 12 Gm., white cells 14,100. Blood sulfanilamide was 7.5 mg. per hundred cubic centimeters. Gonococci were cultured from both the urethra and the cervix. The blood Wassermann test was negative. Urine examination was negative.

The patient was given 33 Gm. of sulfapyridine between October 13 and 21. The blood sulfapyridine content on October 18 was 5.8 mg. per hundred cubic centimeters. Cervical and urethral cultures taken two days after the sulfapyridine was discontinued were still positive for gonococci. In view of the unsatisfactory results of sulfonamide therapy, it was decided to give her fever therapy.

On October 30, after routine preparation, she was given fifteen hours of hyperthermia at 41.5 C. She withstood this procedure very well except for persistent vomiting. Cervical and urethral cultures taken on November 1, 2, 3 and 6 were negative for gonococci. She was discharged on November 6, free from symptoms.

The patient returned to the hospital on November 24 complaining of numbness and weakness of her legs and feet. These symptoms had appeared two weeks after fever treatment and were accompanied by severe pains in her lower back and legs, but they did not prevent her from working. The neurologic examination was negative, except for loss of the achilles reflexes, weakness of the legs and feet and unsteadiness of gait. There were no sensory changes. She returned two weeks later for lumbar puncture. The spinal fluid showed a positive Pandy test and no cells. The total protein was 240 mg. per hundred cubic centimeters.

At the time of her last examination, April 1, complete recovery had taken place and the total protein content of the spinal fluid was 30 mg. per hundred cubic centimeters.

CASE 6.—L. A., a man aged 46, was admitted to the Strong Memorial Hospital on Jan. 2, 1940, for treatment of tabes dorsalis with fever therapy. He gave a history of a penile lesion in 1924, which was treated with mercury inunctions and some medication by mouth over a period of three months. During the past four years he complained of sharp shooting pains in his legs, difficulty in starting the urinary stream, and incontinence of the urine at night. He had noted no disturbances of gait.

The neurologic examination was negative except for unequal pupils, which reacted poorly to light and in accommodation. The tendon reflexes were normal and there was no disturbance of deep or superficial sensibility. Physical examination was not remarkable.

Examination of the blood revealed 12.8 Gm. of hemoglobin, 3,950,000 red blood cells per cubic millimeter and 11,400 white blood cells. The differential count was normal. Urine and stool examinations were negative. The blood Wassermann test with both antigens and the Kahn test were 4 plus. Lumbar puncture yielded a clear, colorless fluid under normal pressure. There were 10 lymphocytes per cubic millimeter. The total protein content of the spinal fluid was 45 mg. per hundred cubic centimeters.

On January 5 he was given fifteen hours of fever at 41.5 + C. without complications. Following the fever treatment he was up and about the division and was discharged January 10.

He returned to the clinic February 9 complaining of weakness of his legs and difficulty in walking. The onset of his weakness was noted following his discharge from the hospital January 10. Over a period of three or four days the weakness rapidly progressed to a point where he was hardly able to walk, unable to climb stairs and unable to get out of a chair without helping himself with his arms, and it was impossible for him to stand on his toes. At no time was there severe pain in his back or legs. Paresthesias were present over the lower legs and feet.

The neurologic examination at this visit was the same as previously recorded except for absence of the right achilles reflex and diminution of the left. He walked with a waddling type of gait. He was unable to get out of a chair without helping himself with his upper extremities. It was impossible for him to climb stairs. Spinal fluid was obtained at the time of this examination, which showed 2 lymphocytes per cubic millimeter and a total protein content of 100 mg. per hundred cubic centimeters.

At the time of his last examination, May 11, there was considerable improvement in the muscular weakness of the lower extremities. The gait was practically normal. The achilles reflexes were absent. Total protein content of the spinal fluid was 45 mg. per hundred cubic centimeters.

Another case which came under observation recently might be briefly mentioned at this time:

A man aged 36 was seen in consultation because of weakness of the legs. His illness began two months previously with pains and tingling sensations in his legs. These symptoms were followed by progressive weakness of his legs which made walking difficult and climbing stairs almost impossible. There was no history of a febrile illness or ingestion of drugs prior to the onset of the neurologic symptoms.

Examination revealed marked weakness of the musculature of the lower extremities without atrophy. He was able to walk unassisted, but climbing stairs was difficult and he was unable to elevate the heels from the floor. The lower tendon reflexes were absent. There was no nerve or muscle tenderness and no sensory changes. The only abnormality of the spinal fluid was a total protein value of 200 mg. per hundred cubic centimeters. This case presented the same clinical picture as the cases already described and is regarded by us as a spontaneous case of the syndrome under discussion.

COMMENT

The six cases reported can be summarized together from the time the fever treatments were given. Each patient was given fifteen hours of fever at 41.5 C. without any unusual complication at the time of treatment or immediately thereafter. In each case there developed within a period of from ten to sixteen days (except in case 6) following fever treatment a neurologic syndrome, unaccompanied by fever, which was remarkably constant. The most constant feature was motor disturbances involving the muscles of the pelvic girdle and lower extremities resulting in a waddling type of gait which was not unlike that seen in progressive muscular dystrophy. Severe radicular pains, muscle nerve tenderness and mild dyesthesias occurred in several of the cases. In no instance were there symptoms referable to the cranial nerves or sphincters. The positive neurologic signs in all cases were limited to the lower half of the body and consisted of muscular weakness resulting in a waddling gait, diminution or absence of the tendon reflexes, minimal disturbances of deep and superficial sensation, and nerve tenderness. Three of the patients complained of marked hyperhidrosis of the feet. Spinal fluid examination in six cases yielded a normal spinal fluid except for an increase in the total protein content ranging between 100 and 240 mg. per hundred cubic centimeters without any increase in the number of cells.

The analysis of these cases, aside from the similarity of the neurologic syndrome, reveals two common factors: first, a prolonged fever treatment of fifteen hours at 41.5 C. and, second, the onset of the neurologic symptoms at a definite time interval ranging between eleven and sixteen days after the treatment. Three patients in the series had taken fairly large amounts of sulfanilamide or its derivatives without evidence of toxic manifestations which could be attributed to the drug or the disease. The drug in case 1 had been discontinued for eight weeks before fever treatment was given. In case 2 it had been stopped two weeks before, and in case 5 it was discontinued a few days before fever therapy was given. Two patients had primary syphilis but only one showed a weakly positive spinal fluid Wassermann reaction for five weeks.

About the time at which we encountered the second case a somewhat similar one was reported by Ornsteen and Furst. Their patient had received about 130 Gm. of sulfanilamide over a period of about thirty-five days for the treatment of gonorrheal infection. About two weeks after the drug was discontinued he was given approximately four hours of fever therapy between 106 and 107 F. He felt much improved and gained weight until one month later, when he noticed that his hips and legs were growing increasingly weaker. He did not complain of pain in his limbs but did note patchy numbness and paresthesia. The chief neurologic signs were waddling gait, weakness of the dorsiflexors of the left foot, loss of the abdominal and left cremasteric reflex, absent achilles reflexes, hypo-active knee jerks, tenderness of muscles, and normal sensation with the exception of diminution of pin point perception below the middle third of the legs. Sulfanilamide was not detected in the blood. Examination of the spinal fluid was essentially negative. The patient left the hospital greatly improved one month after his admission because of the neurologic disorder. They concluded that this was a case of toxic neuritis with a progressive muscular dystrophy-like picture probably resulting from excessive ingestion of sulfanilamide.

The case described by Ornsteen and Furst and our cases 1, 2 and 5 were similar in many respects. The fact that fairly large amounts of sulfanilamide had been administered in these three cases made it seem logical to conclude that the drug alone, or its use prior to the fever treatment, was in some way responsible for the neurologic changes.

Prior to the advent of sulfanilamide and with routine fifteen hour treatments, a neurologic complication of the type described has not been observed in our clinic, where various amounts of fever at high temperatures have been administered in 1,100 cases. The follow-up on all of these 1,100 cases has been adequate enough to warrant the belief that no similar cases have resulted from the technic of the treatment. In recent literature many toxic effects of sulfanilamide have been described, but as a rule they appear during the administration of the drug and subside when it is discontinued. However, cases have been reported in which the toxic manifestations have been delayed. Lockwood⁶ mentioned a case in which severe hemolytic jaundice developed eighteen days after the drug had been discontinued.

In view of the fact that this neurologic syndrome had never been observed to follow either form of treatment when used alone, it was thought that perhaps the combination might in some way be responsible. A few months later, however, following a routine fifteen hour fever, we observed the same syndrome in two cases of primary syphilis and one case of *tabes dorsalis* in which sulfanilamide had never been given. This seemed to exclude sulfanilamide as a causative agent. Likewise the technic of the fever therapy appeared unlikely as the sole cause. In this clinic several hundred cases were treated with prolonged fever, from fifteen to twenty-seven hours at 41.5 C. (106.7 F.), prior to June 1938 without any complication of this type.

Guillain believes that the syndrome which he described is of infectious origin, presumably a neurotropic virus. He also stated that in some cases it had been noted that the polyradiculoneuritic syndrome developed often after a suppurative infection. He was of

the opinion that in such instances a neurotropic virus plays the principal role but acquires its virulence as a result of the primary illness. At least one virus disease, herpes simplex, seems to be activated by the febrile state (Carpenter, Boak and Warren⁷). The herpetic vesicles containing the virus develop in about 60 per cent of all cases in which fever treatment is administered. The lesion starts as an erythematous patch on the face, usually about the nose or mouth, about twenty-four to thirty-six hours after the fever. Within twelve hours a papule develops which becomes a vesicle, then a pustule and finally a dry crust, which falls off in a week or ten days, leaving no scar. Herpes simplex developed in three of the six cases under discussion.

There were several features about our cases which suggested an infectious (virus) etiology. Most important of these was the latent period between the fever therapy and the development of the neurologic symptoms. This period was fairly uniform in the six cases reported and might well represent the incubation period of a virus present in the body which became activated by fever therapy (much as seems to be the case with the herpes simplex virus). We were also impressed by the fact that all the cases were encountered over a period of slightly less than two years, an observation which might indicate that a virus capable of producing the neurologic disorder was prevalent during this time. Additional evidence in favor of this idea is the increase in number of spontaneous cases which we have observed during the same period. These cases differed from those under discussion in that the paralysis was more extensive, the course more protracted and the protein content of the spinal fluid considerably higher. We might regard the cases discussed as mild or abortive forms of the syndrome. In the cases reported, animal inoculations with spinal fluid gave negative results. In 1936 Gilpin, Moersch and Kernohan⁸ reported a large series of cases of polyneuritis with albuminocytologic dissociation and called attention to the increasing incidence of the disorder. It was their impression that the condition was due to a virus that had a predilection for the peripheral neuron.

The prognosis in these cases has been favorable for recovery. Pain and tenderness of the nerves and muscles subsided within a week or two. However, the return of muscular power takes much longer and it is usually from four to six months before the gait returns to normal. The abnormality of the spinal fluid is likewise slow in clearing.

Treatment of these cases consisted of the usual therapy for cases of polyneuritis due to other causes (relief of pain, rest of muscles and so on).

SUMMARY AND CONCLUSIONS

1. Six cases of polyradiculoneuritis with hyperalbuminosis of the spinal fluid followed the use of sulfanilamide and general hyperthermia.

2. Analysis of these cases would seem to eliminate sulfanilamide and hyperthermia per se as the cause of the syndrome.

3. It would seem that the disorder is the result of the activation of some infectious agent, perhaps a virus, by the fever.

7. Warren, Stafford L.; Carpenter, Charles M., and Boak, Ruth A.: Symptomatic Herpes, a Sequela of Artificially Induced Fever, *J. Exper. Med.* 71: 155-168 (Feb.) 1940.

8. Gilpin, Sherman F.; Moersch, Frederick P., and Kernohan, James W.: Polyneuritis, *Arch. Neurol. & Psychiat.* 35: 937 (May) 1936.

6. Lockwood, John S.; Coburn, Alvid F., and Stokinger, H. E.: Mechanism of the Action of Sulfanilamide, *J. A. M. A.* 111: 2259 (Dec. 17) 1938.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. DE JONG AND DRs. GARVEY, JONES
AND WARREN

DR. LOUIS CASAMAJOR, New York: Much confusion has existed concerning the term "Landry's paralysis." It was early believed to be a form of subacute poliomyelitis but later work showed that progressive ascending paralysis was not occasioned by a progressive ascending inflammatory reaction in the anterior central gray matter. The clinical course of these cases with complete recovery of a large majority taught that the lesion was not one of destruction of the anterior horn cells. Obviously some reversible process must exist as the basis of acute ascending paralysis. The pathologic observations which Dr. DeJong reports in his cases were practically identical with those of the two cases I reported in 1919. The differences were of degree and not of kind. I was convinced that the primary lesion was an inflammatory one in the arachnoid affecting primarily the nerve roots where they run in the arachnoid. The peripheral nerve changes and those in the anterior horn and spinal ganglion cells are secondary to interruption of nerve fiber function by the arachnoid inflammation. The situation was somewhat similar to tabes as described by Nageotte and it is interesting that in tabes with a productive arachnoiditis the changes are almost entirely in the sensory roots. In the acute ascending paralysis there is likewise an arachnoiditis but not a productive one, and for some unknown reason the changes are more in the anterior roots. When my cases were reported I was unaware of the article of Guillain-Barré and Stöhl, which had been published three years earlier. Spinal punctures could not be done in my cases as they were observed under conditions of active warfare, and had the spinal fluid been obtained there were no facilities for determination of total protein. In the cases seen more recently the albuminocytologic dissociation described by these authors was present in all. Dr. DeJong included in his paper two cases in which, for good reasons, lumbar puncture was not done. In the second case of his series there was a definite albuminocytologic dissociation. The existence of the high protein and low cell count in the spinal fluid is to my mind a valuable finding. I feel it is the spinal fluid expression of the inflammatory changes in the arachnoid which I believe to be the basic cause of the condition. The existence of such a reaction differentiates the condition from poliomyelitis on the one hand and peripheral neuritis on the other. Were this a real anterior horn cell degeneration due to poliomyelitis, one would certainly expect to find the meningeal reaction which gives the increase of cells with not such a great increase of protein. That fact alone proves that the pathologic change responsible for this condition exists inside the dural sac. The term "Landry's paralysis" could be dropped without much loss to our nomenclature.

DR. PETER BASSOE, Chicago: I wish Dr. De Jong had taken more time to describe that type of lesion. It perhaps represents a clinical entity which we will understand better when we know more about viruses. When it comes to his discussion of terminology, I cannot follow him. The term "Landry's paralysis" is obsolete and confusing, whether Landry's case was one of beriberi, as claimed by Dr. Madelaine Brown, or a cord infection similar to the one described by Dr. De Jong. The term "acute ascending paralysis" (ascending must mean ascending, whether one thing or another; we can't change the English language) is useful as designating a syndrome which is fairly common on account of the segmented structure of the cord. Any disease starting in the lower part of the cord with sufficient momentum to travel upward may produce an ascending paralysis, and I don't see any reason why we should not call it all ascending paralysis, which of course makes it a syndrome only. And I don't see why we shouldn't say that, when ascending paralysis is caused by poliomyelitis, that is also ascending paralysis. Less common are the kinds of myelitis described by Dr. DeJong today. Perhaps they are commoner than we think. Then there are the kinds of spinal root and ganglion inflammation that have been described by Pette and Környey and more recently by Peters and Scheid. Rabies, rabies vaccine paralysis and tick paralysis may be acute ascending; and we may have ascending leptomenigeal,

dural and epidural inflammations and so on. The day I left home I saw for the first time Wilson's magnificent two volume textbook. I looked up what he said about Landry's paralysis, and as most of you may not yet have seen the book I will quote some of his statements: "As a technical term Landry's paralysis lacks precision, etiological or pathological, and its clinical worth is a little dubious. The name lingers on, none the less, bearing witness to the fact that clinical types of acute ascending paralysis are not uncommon and that knowledge of their causation is still at times rudimentary." Wilson considers it a mistake to confine the syndrome to the motor system. He included poliomyelitis, also ascending myelitis, in the spinal disorders. He says "As has often happened in medicine, the first conception has been widened and a host of cases included of which perhaps only a few strictly conform to it. On the pathologic side, too, variations have been numerous enough to render a unitary acute ascending paralysis impossible." Then finally he adds something pertinent to what Dr. De Jong has said today, namely "For some obscure reason several writers today seek to restrict Landry's paralysis to the acute ascending toxicosis of ventral horn cells" (without inflammation).

DR. A. M. ORNSTEEN, Philadelphia: In the group of cases reported by Dr. Garvey and his co-workers there can be no question about its similarity to the Guillain-Barré syndrome because of the acute onset with a uniformity of clinical picture as he described involving the lower extremities and the cytoalbumin dissociation which has been consistently held as a differential finding in this form of multiple or polyneuritis. In an experience of 1,150 cases of fever therapy, given I presume under similarly controlled conditions over a period of ten years, Dr. Garvey and his co-workers have not seen such a complication, but in the past two years they have seen six cases under identical conditions of the fever treatment with a period of incubation of from ten to sixteen days, followed by weakness of both lower limbs, pain in the back, severe in some cases, various reflex and sensory changes and with the spinal fluid feature already mentioned. They did not conclude that fever therapy was the cause of it; neither could they conclude that sulfanilamide would produce the neuritis, for obvious reasons, and their conclusion that the virus was activated by fever I believe is acceptable unless some one can give a reason why such a situation does not occur occasionally in the situation in which patients harbor a virus and their resistance to that virus is altered by certain physical factors. It has been well known that neuritis is often attributed by the patient and the physician to a certain physical factor, exposure frequently the offending factor; and there are people who still believe that such a common peripheral neuritis as Bell's palsy is caused by exposure, whereas others believe that the particular individual who develops a Bell's palsy must have some factor in the background which makes that nerve vulnerable to exposure; hence Dr. Garvey's interpretation that activation of a virus in the host may be produced under certain conditions, at present not understood, by fever. Since it did not happen in the first eight years of the decade of his survey and it has in the last two years, it would be interesting to determine whether or not in his community there were an equal number of cases, not just the one other case which he saw in which no sulfanilamide or fever therapy was given, that showed a development of the Guillain-Barré syndrome. That would be more convincing; the increased incidence of the disease would explain the increased number of carriers of the virus and, under certain conditions, such as hyperpyrexia in Dr. Garvey's cases, exposure to cold, or a background of vitamin deficiency, infectious polyneuritis may be precipitated.

DR. FREDERICK P. MOERSCH, Rochester, Minn.: We have more or less dropped the term "Landry's paralysis" because we do not know the etiology of the condition. Once we discover the exact etiology of "Landry's paralysis" a reclassification of these conditions will be easier. As far as I know, we have seen no case of peripheral neuritis or polyradiculoneuritis resulting from sulfanilamide therapy. We have observed cases of peripheral neuritis resulting from preparations related to sulfanilamide. The fact that neurologic complications so rarely follow the use of sulfanilamide I believe is good evidence that in Dr. Garvey's cases the sulfanilamide

probably had no relation to the onset of the symptoms. Regarding fever therapy, we have observed one instance of polyradiculoneuritis following from therapy. It was interesting that this patient, because of an acne, had received a preparation containing tin just prior to the fever therapy and sulfanilamide. We were unable to determine in our own minds whether the neuritis or polyneuritis was due to tin, to fever or to some unknown factor. Some time later when we went through what seemed to be a wave of polyradiculoneuritis we instituted fever therapy in these cases with poor results, and we concluded that fever therapy in cases of polyneuritis was rather harmful. Dr. Krusen of our staff has called to my attention a report by Dr. Gwynn of Washington, who reported four cases of peripheral neuritis following fever therapy. At the same time, in the same city but in another hospital, and using a little different type of fever therapy, there were observed fourteen cases of peripheral neuritis following fever therapy. I have seen the records of some of those patients and I am inclined to believe that they represent a polyradiculoneuritis as described by Dr. Garvey and his co-workers. The large number of cases of peripheral neuritis occurring in one locality suggests the possibility of some infectious basis. As noted by Dr. Garvey, the usual sequence of events in a case of polyradiculoneuritis is an infection, a latent period, and then the development of a polyradiculoneuritis, suggesting the presence of a common denominator as a virus. There are many cases in which no infection or infectious history is obtainable, and I have been wondering whether polyradiculoneuritis may not after all be another syndrome rather than a disease entity resulting from a specific virus.

DR. A. E. BENNETT, Omaha: I should like to inject into this discussion of cases involving the so-called Landry syndrome the possibility that some of them resemble curare poisoning. Of the cases I have seen, an almost pure flaccid motor paralysis develops in most and death occurs from asphyxia. However, when recovery occurs it is rapid. In one recent case recovery occurred within a few days after the paralysis became complete, including the respiratory muscles. Prostigmine and thiamine were used in treatment. It seems that there is some evidence to show that perhaps faulty neuromuscular function with a lack of acetylcholine may be a factor in this syndrome. With respect to Dr. Garvey's cases, almost any clinic that has given large numbers of fever therapy treatments has seen this complication. Dr. Garvey's patients were given long fever therapy heatings of ten hours or more. I doubt the idea of virus infection being responsible for this disorder. Anoxia and thiamine deficiency are more likely causative factors. Weaver, formerly of Ohio State and now of Detroit, has definitely produced peripheral neuritis in animals with fever therapy and anoxia. Since we discovered this condition we have given all our patients prophylactically large doses of thiamine and throughout the long heatings they get oxygen. As Dr. Moersch told you, in the large number of treatments given at the Mayo Clinic they have seen only one case, and it has been routine for Dr. Krusen to use continuous oxygen inhalation with fever therapy. It may be that sulfanilamide is also a factor in the production of anoxia and finally polyneuritis.

DR. NORMAN JOLLIFFE, New York: I should like to bring out a point that may account for the development of polyneuropathy following fever therapy. It was shown several years ago by Cowgill that the vitamin B₁ requirement increased with an increase in total metabolism. The administration of fever therapy over a period of ten hours every day or every other day must increase the total metabolism markedly, and with it a parallel rise in the thiamine hydrochloride requirement. It would not be inconceivable that the vitamin B₁ requirement of these individuals was doubled, and unless dietary precautions were taken to increase the B vitamins it is likely that with the increased requirement due to fever therapy their diet was inadequate in vitamin B₁. The ten to fourteen day period mentioned by Dr. Garvey could as well be the time required to develop a polyneuropathy due to a vitamin B₁ deficiency as to an incubation period of an infection. I should like to ask a question concerning the cell counts in Dr. Garvey's patients. I believe that in about one half of his patients

absolutely no cells were found in the spinal fluid. Did he not mean to indicate that there was no increase in cells?

DR. PAUL C. BUCY, Chicago: Dr. Joliffe, I should like to ask whether or not you would expect this alteration in protein content in the spinal fluid with thiamine hydrochloride deficiency?

DR. JOLLIFFE: Certainly not, as a rule. We have, however, seen increased protein in the spinal fluid in patients having thiamine hydrochloride deficiency, though it occurs rarely. Whether the increased protein was due to B₁ deficiency or not, I have no proof. Since thiamine hydrochloride deficiency is not limited to the peripheral nerves but includes changes in the roots and spinal columns as well, it is theoretically possible that an increased protein content might result from thiamine hydrochloride deficiency.

DR. MOERSCH: In a postdiphtheritic polyneuritis in which there is an increase in the total protein, would that fit in with this? I was wondering what your experience might be.

DR. JOLLIFFE: I have never seen an acute postdiphtheritic neuritis, but it would fit in with this explanation.

DR. IRVING J. SANDS, Brooklyn: Those of us who have had the opportunity of following the various types of encephalitis during the past years have been impressed with the increase in the number of patients of the type described by the readers of the last two papers. Dr. De Jong's cases brought to my attention a group of patients we have had the privilege of following in Dr. Riley's division at the Neurological Institute. They have been described as diseases due to virus infection, manifested clinically by an ascending type of paralysis. Those cases which came to necropsy showed a difference in the pathologic condition though clinically they showed an almost identical course. I recall two patients who had a definite ascending paralysis with death resulting in about six to ten days after the onset of the illness. In one patient multiple areas of demyelination were found, and in the other nothing except slight cloudy swelling and chromatolysis were detected. During the past four years I have had the opportunity of following a group of cases at the Kingston Avenue Hospital for Contagious Diseases. They presented a symptomatology as shown by Dr. Garvey's patients. However, they had a much larger total protein in the spinal fluid, usually between 200 and 350 mm. In the majority of these cases there was a history of a mild upper respiratory infection preceding the onset of the neurologic signs. In the past two years we have been giving them large doses of thiamine hydrochloride. It has been my impression that thiamine hydrochloride therapy has made no difference in the speed or the extent of the recovery. What is the etiology of these cases? I believe that it is due to a virus infection, though I have no definite proof. It is the opinion of many who have studied the manifestations of encephalitis and encephalomyelitis that the virus agents comprise a large group like the pneumococci, that eventually these different groups will be differentiated and recognized, and that each type of virus will be proved to have a special predilection for invasion of a particular part of the nervous system producing the different clinical types of neurologic disorders with which we are now familiar clinically.

DR. DONALD SHASKAN, New York: In a period of less than two years we have followed eight cases of the Guillain-Barré syndrome in Dr. Foster Kennedy's service at Bellevue. I should like to ask Dr. Garvey two questions: Guillain has stipulated that from 1,000 to 2,000 mg. of total protein was necessary for the diagnosis of this syndrome, and I wondered what Dr. Garvey thinks of this quantitative differentiation as a factor in diagnosis. The second question is Why should no virus have been recovered in any of these cases, either Dr. Garvey's cases or any cases in the literature?

DR. A. M. RABNER, Brooklyn: I had not intended discussing these cases until some of the discussers attempted to blame fever therapy for the development of these clinical syndromes. On a number of occasions spinal fluid examinations of patients who did not have any evidences of polyneuritis, polyradiculoneuritis or meningo-encephalomyelitis, who in the course of an upper respiratory infection seemed somewhat drowsy, had spinal fluid study performed which revealed an

increased total protein. We also know that virus infections causing the so-called common cold produce a varying type of clinical picture. Sometimes there is only a tracheitis, at other times more widespread involvement of the respiratory apparatus. In other words, we know that virus infections that do not involve the central or peripheral nervous system may produce a protean type of implication of the system in general. Some years ago when Dr. Strauss and I reported a group of these cases we called them, for want of a better name, myelodradiculitis. In reviewing the literature we found reports of similar clinical syndromes from all over the world with many names attached to them, indicating varying diffuse anatomic involvement, at times limited to the brain, at other times affecting also the meninges, sometimes limited only to the cord and often implicating all the structures from the peripheral nerves up the roots, to the brain. The names given to these syndromes were usually purely anatomic designations of the structures involved. One of our patients subsequently developed a parkinsonian syndrome and this suggests an etiology similar to that causing epidemic encephalitis. Here then Dr. Garvey reports a group of six cases occurring within a short period of time under the same type of fever therapy regimen that has been given to their patients in previous years. Now for the first time six cases appear with this clinical picture. To blame the fever therapy for this I think is a far fetched speculation. These are undoubtedly cases in which there was a virus infection of the nervous system during the period fever therapy was being administered.

DR. RALPH HAYWARD, Toronto: I want to mention about 150 cases of ascending paralysis that I saw in West China. These cases all seemed to occur in a region of about 20 miles radius. Cities 100 miles away had none at all. The onset was sudden, with a little nausea and vomiting, the symptoms appeared in about five or six hours, and recovery would occur in three or four days. About 5 per cent of the patients died within forty-eight hours. The peculiar thing was that the inhabitants of the city did not seem to be bothered, but after the war with Japan a national university came to our city and the students came down with it in large numbers; I don't know whether it was from eating the same things or from respiratory infection. Just as I came away this April there were several camps for wounded soldiers where the men were coming down in large numbers with this same disease.

DR. RUSSELL N. DE JONG, Ann Arbor, Mich.: It was desirable that my paper on acute ascending paralysis and Dr. Garvey's paper on the Guillain-Barré syndrome be discussed together, because clinically these two conditions are similar and they may represent different stages or degrees of the same disorder. I have been studying a group of cases, seen in the University Hospital in Ann Arbor, which conform closely to those described by Guillain and Barré, but I disagree with the French authors in certain respects. In their terminology of the syndrome they use the word "curable" polyradiculoneuritis. If the syndrome is to be diagnosed by the presence of albuminocytologic dissociation, I am sure that not all cases are curable. I have observed some cases that conformed to the descriptions of Guillain and Barré but had a chronic course and others that terminated fatally. The condition is certainly more than a peripheral neuritis, as in some cases a facial paralysis has been noted, others have shown evidence of a brain stem or bulbar paralysis, and papilledema has been noted in certain instances. Paralysis of the bowels or bladder is not unusual. The cases that terminate fatally are similar to those that I have described today as cases of acute ascending paralysis, and it is my impression that these all are members of the same group of disorders. If that is the case, we shall have to enlarge or broaden our concept of the term "polyradiculoneuritis" as described by Guillain and Barré, noting that the prognosis is not favorable in all cases—not all are curable, and some terminate fatally.

DR. PAUL H. GARVEY, Rochester, N. Y.: In reply to Dr. Ornstein, at the present time we have two patients in the hospital that have total protein contents one of 800 and one of 600, and since this paper was written we have had three more cases following fever therapy. Perhaps this protein is

due to edema and vascular congestion at the time of the fever treatment. However, we have done routine punctures on the last three patients that developed the same syndrome and the total protein content of fluid was within normal limits three days after the treatment, so presumably that abnormality develops later and cannot be directly related to the fever. It was suggested by Dr. Bennett that it was due to anoxia and perhaps to the fever treatment. Prior to two years ago we treated patients for twenty-seven hours and many patients have been treated more than fifteen hours without anything of this sort developing, so that I should think if it were on that basis these cases would have occurred before two years ago. With regard to this being a vitamin deficiency or the development of an acute deficiency, it has been our experience that large doses of thiamine hydrochloride have not been effective in the treatment of these cases. In the neuritis associated with chronic alcoholism, which is a good example of a deficiency neuropathy, the total protein content of the spinal fluid is not appreciably elevated. The cell counts were taken from the records recorded by the house officers. Of course from ten to fifteen years ago a cell count of ten was said to be normal; now we know that anything above five is considered abnormal, so that so far as the chart was concerned I would just as soon have one, two, three or four cells on that chart as none. Guillain in his recent article insists that 1 or 2 Gm. of protein must be present in the spinal fluid in order to make the diagnosis. I think it seldom attains that level. He mentioned in his article that when the spinal fluid protein is lower than 1 or 2 Gm. they must be considered as abortive cases. It is interesting that about two weeks ago in *THE JOURNAL* Stone and Aldrich reported two cases of this syndrome in which albuminocytologic dissociation was a late development.

THE EFFECT OF DISTENTION OF ABDOMINAL VISCERA

ON THE CORONARY BLOOD FLOW AND ON
ANGINA PECTORIS

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AND

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The incidence of anginal pain following the ingestion of food has been commented on by most of the writers on angina pectoris, beginning with Heberden,¹ who stated that "those who are afflicted with it are seized while they are walking, and more particularly if they walk soon after eating." Osler,² in his monograph on angina pectoris, states "Of the exciting causes there are three important elements: muscular exertion, mental emotion and digestive disturbances. . . . As an attack ends, the patient may belch quantities of gas or pass flatus from the bowel, both with apparent great relief." So marked is the association of pain with upper digestive tract symptoms that Verdon³ and later the Jacksons⁴ considered that the pain was of neuromuscular origin, consequent on gas under pressure in a hollow viscus.

The increased incidence of anginal pain after meals is explained in part by the increased work required

Read before the Section on Practice of Medicine at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Heberden, William: *Some Account of a Disorder of the Breast*, M. Tr. College of Physicians 2: 59-67, 1786.

2. Osler, William: *Lecture on Angina Pectoris and Allied States*, New York, D. Appleton & Co., 1897.

3. Verdon, Walter: *Angina Pectoris*, London, Baillière, Tindall & Cox, 1920.

4. Jackson, D. E., and Jackson, Helen L.: *Experimental and Clinical Observations Regarding Angina Pectoris and Related Symptoms*, J. Lab. & Clin. Med. 21: 993-1006 (July) 1936.

of the heart during digestion. This of itself demands an increased coronary flow, and the vessels may not be able to supply this demand even without the added factor of exertion. But this does not explain the effect of gaseous distention of the stomach in causing anginal attacks or the relief offered by belching. And it does not explain the influence of abdominal distention.

There is both clinical and experimental evidence to indicate a reflex vasoconstriction of the coronary arteries consequent on some stimulus arising in the viscera or elsewhere. Huchard⁵ predicated a reflex angina, and Daniélopou⁶ considered that a coronary vasoconstriction could result from a stimulus originating in the thoracic cavity. Anrep⁷ showed a reflex decrease in coronary flow with an increase in the intracerephalic pressure, and Stella⁸ showed that this was produced by means of the carotid sinus. Manning, McEachern and Hall⁹ showed that there was a reflex vasoconstriction following sudden occlusion of other coronary branches. De Takats, Beck and Fenn¹⁰ presented evidence indicating a reflex vasoconstriction of coronary arteries following pulmonary embolism. Von Bergmann¹¹ showed a reflex vasoconstriction of the coronary arteries following gastric distention, and Rein¹² showed that there was some constant vagal tone present in the coronary arteries and that constriction resulted from vagus stimulation.

There would seem to be abundant experimental evidence to indicate that stimulation of the vagus does result in vasoconstriction of the coronary vessels. This is amply reviewed by Anrep¹³ and by C. W. Greene.¹⁴ As Greene states, however, the reaction of the coronary vessels to stimulation cannot be predicted because of the close morphologic and physiologic association of the vasoconstrictor and vasodilator pathways. In order to prove the hypothesis of vagal origin of the vasoconstrictor fibers, he performed a series of crucial experiments in which he completely severed the vagal neurons from the coronary vagosympathetic pathways. This he accomplished by sectioning the vagus at its exit from the jugular foramen and carried on a series of physiologic experiments after degeneration of the vagus fibers. Dogs with such section of the vagus showed a loss of coronary constriction on cervical vagal-sympathetic stimulation.

In some earlier work with Prof. C. W. Greene in 1925, one of us had observed a decrease in coronary flow on distention of the stomach or the free abdominal cavity, measuring the flow with a Morovitz cannula. The results were not constant and were not published because of the fear that a factitious element might be present. The work was later repeated by Gilbert and

Fenn with similarly inconclusive results. In both cases, lack of constant results can be ascribed to the type of anesthesia used, to the fact that anesthesia was carried to the point at which reflexes would tend to be abolished, and to too strong a stimulus. The Morovitz cannula method is also not as well adapted to this work as is the Rein thermostromuhr. A change in the relative position of the heart may mechanically cause a decrease in flow.

Hinrichsen and Ivy¹⁵ also were unable to find a vasoconstrictor effect on the coronary artery with visceral stimulation but found it possible to show a vasodilator effect.

A short time ago we¹⁶ reported on some experimental work in dogs which indicated that moderate distention of the stomach could cause a reflex constriction of the coronary arteries. Under light anesthesia a thermostromuhr was applied to the circumflex branch of the left coronary artery. The chest was closed and continuous photographic records were made of the coronary flow, together with blood pressure and pulse readings.

TABLE 1.—Experiments on Visceral Distention

Part Distended	Number	Coronary Artery Flow		
		Decreased	Increased	No Change
			(Before atropine: 2 mg./Kg.)	
Stomach.....	12	8	1	3
Gallbladder.....	7	2	2	3
Peritoneum.....	6	3	3	0
(After atropine: 2 mg./Kg.)				
Stomach.....	11	1	5	5
Gallbladder.....	6	1	2	3
Peritoneum.....	4	0	3	0
Unanesthetized Dogs				
		(Before atropine)		
Stomach.....	3	3	0	0
		(After atropine)		
Stomach.....	2	0	1	1

Moderate distention of the stomach caused a decrease in the coronary flow without fall in blood pressure. The decrease was greater when the distention affected primarily the cardiac end of the stomach, as was observed by von Bergmann¹¹ in similar experiments. Section of the vagus or administration of atropine abolished the reflex. Distention of the free abdominal cavity with air also resulted in a decreased coronary flow, which again did not appear after vagus section or atropine. Since these experiments were reported, a similar series of experiments have been made on unanesthetized dogs which had previously had a thermostromuhr attached to the circumflex branch of the coronary artery under aseptic conditions, with perfect recovery. The results were essentially the same.

The results of the distention of the stomach and abdominal cavity in the anesthetized dogs and the results of the distention of the stomach in the unanesthetized dogs before and after the injection of atropine are shown in table 1. The results of the gallbladder experiments are not conclusive as far as they have been carried out. The work will be amplified and reported on later.

5. Huchard, Henri: *Traité clinique des maladies du cœur et des vaisseaux: Leçons de clinique et de thérapeutique des cardiopathies artérielles*, ed. 2, Paris, Gaston Doin & Cie, 1893.

6. Daniélopou, D.: *L'angine de poitrine et l'angine abdominale*, Paris, Masson & Cie, 1923.

7. Anrep, G. V.: *Lane Medical Lectures: Studies in Cardiovascular Regulation*, Stanford University, Calif., Stanford University Press, 1936.

8. Stella, G.: Some Observations on the Effect of Pressure in the Carotid Sinus upon the Arterial Pressure and upon the Coronary Circulation, *J. Physiol.* 73: 45 (Sept.) 1931.

9. Manning, G. W.; McEachern, C. G., and Hall, G. E.: Reflex Coronary Artery Spasm Following Sudden Occlusion of Other Coronary Vessels, *Arch. Int. Med.* 64: 661-674 (Oct.) 1939.

10. de Takats, Geza; Beck, W. C., and Fenn, G. K.: Pulmonary Embolism, *Surgery* 6: 339 (Sept.) 1939.

11. Von Bergmann, G.: Das "Epiphrenale Syndrom," Seine Beziehung zur Angina Pectoris und zum Kardiospasmus, *Deutsche med. Wchnschr.* 55: 605-609 (April 15) 1932.

12. Rein, Hermann: Die Physiologie der Herz-Kranz-Gefäße, *Ztschr. f. Biol.* 92: 115-127, 1931.

13. Anrep, G. V.: The Regulation of the Coronary Circulation, *Physiol. Rev.* 6: 596-629 (Oct.) 1926.

14. Greene, C. W.: The Nervous Control of the Coronary Circulation, *South. M. J.* 29: 478-485 (May) 1936.

15. Hinrichsen, Josephine, and Ivy, A. C.: Effect of Stimulation of Visceral Nerves on Coronary Flow in Dogs, *Arch. Int. Med.* 51: 932-937 (June) 1933.

16. Gilbert, N. C.; LeRoy, G. V., and Fenn, G. K.: The Effect of Distention of Abdominal Viscera on the Blood Flow in the Left Circumflex Coronary Artery of the Dog, *Am. Heart J.*, to be published.

In order to extend these observations on gastric distention to patients with angina of effort we had recourse to the method devised by Levy.¹⁷ This method consisted in allowing a patient to breathe an oxygen-poor mixture until pain occurred. It was safe, because at

TABLE 2.—*Abstracts of Histories of Patients*

Name.....	1. J. B.	2. G. L.	3. A. K.
Age.....	70 years	51 years	57 years
Diagnosis.....	Arterio- sclerosis; heart disease	Syphilitic aortitis; arterio- sclerosis; heart disease	Syphilitic aortitis; arterio- sclerosis; heart disease
Blood pressure.....	203/110	150/68	160/74
Heart size.....	51%	42%	55%
Left ventricle.....	9.8 cm.	10.0 cm.	12.0 cm.
Electrocardiogram: PR...	0.28	0.18	0.22
QS...	0.05	0.06	0.06
QT...	0.40	0.36	0.34
T ₁ ...	Inverted	Low	Low
T ₂ ...	Low	Normal	Low
T ₃ ...	Inverted	Normal	Normal
ST...	Slightly depressed	Normal	Normal
Duration of angina.....	3 years	4 years	3 years
Severity.....	++++	++	+++

the first sign of pain 100 per cent oxygen was administered with immediate and complete relief. It was of interest that the patients stated that after a spontaneous attack of angina they felt some depressing effect for hours. However, after these induced attacks, followed at once by oxygen administration, they stated that they felt better than before the attack.

The method as used by us consisted in allowing the patient to breathe 10 per cent oxygen and 90 per cent nitrogen while lying quietly in bed and after a thirty minute rest period. The patient was instructed to indicate the moment he felt his typical anginal pain. The procedure was repeated on successive days until the patient became accustomed to the method and the control pain time became stabilized. After the control

TABLE 3.—Experiments on Conscious Dogs

Thermostromuhr on Circumflex Branch, Left Coronary Artery Change in Coronary Flow		
Dog	Effect of Feeding	Time After Feeding
T-1.....	— 5%	5 min.
	— 10%	20 min.
	+ 5%	15 min.
	+ 3%	15 min.
	+ 10%	15 min.
	0%	10 min.
T-3.....	+ 6%	10 min.
	— 5%	20 min.
	+ 5%	15 min.
T-5.....	0%	10 min.
	+ 8%	15 min.

Note: Each percentage change listed represents a separate feeding, on separate days.

pain time had been determined, the procedure was repeated ten minutes after the ingestion of a moderately large meal and the pain time again recorded. Subsequently the second procedure was repeated after atropine in doses of one-fiftieth grain (0.0013 Gm.) had been injected intramuscularly just preceding the

meal. The period required to produce pain in this instance was recorded. Several determinations of each of these pain times were made.

The patients, three in number, were hospitalized for the several days required for the investigation, were known subjects of anginal pain and were removed from all medication for several days preceding the tests. They were selected from a large group of patients because of the constant character of their angina. All three complained initially that exertion after meals produced pain much sooner than was usual at other times. These three also reported that ingestion of certain foods, such as cabbage, sauerkraut, onions and other indigestible foods, was generally followed by an attack of angina. In all of them the angina, of course, varied in degree, but the more severe attack was of the classic Heberden variety. Each of the patients, prior to entering the hospital for this investigation, had obtained marked relief from his anginal symptoms by the faithful use of theophylline with ethylene diamine in doses of from 0.6 to 1 Gm. daily. On withdrawal of the drug, each of these patients had a prompt recurrence of frequent

TABLE 4.—*Tolerance of Anoxemia Produced by 10 per cent Oxygen, 90 per cent Nitrogen*

Summary of Data				
Items	Subjects			
	I. J. B.	2. G. L.	3. A. K.	
All tests before eating; average.....	13:10	5:42	11:55	
All tests after eating; average.....	10:45	3:25	7:45	
Change after eating.....	-19%	-40%	-35%	
Tests before eating, after atropine; average	12:40	7:36	
Change before eating, after atropine, average	-3.7%	+33.0%	
Test after eating, after atropine, average..	12:30	6:28	14:42	
Change after eating, after atropine: (Test after eating, after atropine)	in %..	+17%	+57%	+93%
All tests after eating)				
Change after eating, after atropine: (Test after eating, after atropine)	in %..	-5%	+12%	+24%
All tests before eating)				

anginal pain. The pertinent data relative to the patients are shown in table 2.

The effect of the ingestion of food on the pain time is shown in chart 1.

The control pain time is plotted at 100 per cent, no attention being paid to the actual number of minutes required to produce pain. In a similar manner the pain time following ingestion of food and later following ingestion of food plus atropine is plotted in percentages of the control time. The actual time required to produce pain by the respiration of 10 per cent oxygen and the changes produced by food and atropine were quite different in each patient, and these figures are shown elsewhere (table 4).

Patient 1 (J. B.) found that the pain time following the ingestion of food was 19 per cent less than the control time. That is to say, his tolerance for 10 per cent oxygen was reduced by about one fifth. In a similar way patient 2 (G. L.) showed a reduction of 40 per cent and patient 3 (A. K.) a reduction of 35 per cent. We believe that these results demonstrate that the ingestion of a meal considerably increases the susceptibility to anginal pain in these anginous patients.

The effect of atropine on the pain time following the ingestion of food is shown in chart 2. Atropine

17. Lery, R. L.; Bruenn, :
Action of Certain Drugs
Effects of Induced Anoxemi:
Am. Heart J. 19: 639-654 (June) 1940.

W. E.: The Modifying
Digitalis) on the
ronary Insufficiency,

lengthened the after meal pain time of patient 1 by 17 per cent. In comparing the pain time after food and atropine with the control time it will be seen that they are nearly the same. Actually the pain time after food and atropine was 5 per cent less than the control time. Atropine increased the after meal pain time of patient 2 by 87 per cent, which was enough to make it 12 per cent greater than the control pain time. Atropine increased the after meal pain time of patient 3 by 93 per cent and brought it up to 24 per cent above the control time.

Chart 3, in which the pain time after food plus atropine is plotted against the pain time after food alone, shows these results in a somewhat more striking fashion. The results would seem to indicate that atropine successfully interferes with the mechanism that increases the susceptibility to anginal pain after meals. It is our belief that this interference is due to inhibition of vasoconstrictor impulses that are mediated through the vagus nerve.

It has been stated¹⁸ that a considerable increase in the coronary flow follows the ingestion of food. In our own laboratory we were unable to observe any appre-

article in which they show an increase of 86 per cent in the intact conscious dog after atropine.

The effect of atropine alone on the low oxygen tolerance in two of the patients who were investigated is shown in chart 4. With patient 1 atropine alone made

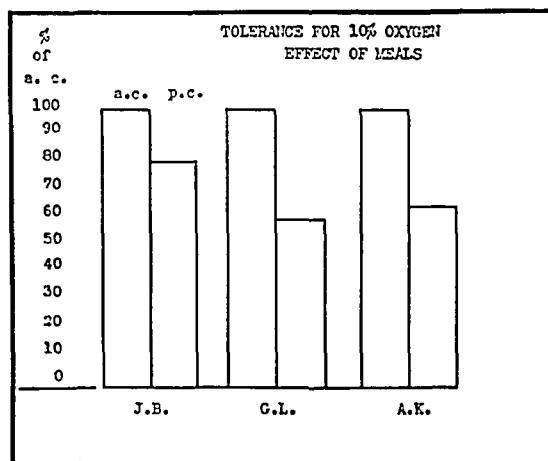


Chart 1.—The time each subject tolerated the 10 per cent oxygen inhalation before meals is represented as 100 per cent in the left hand column of each group, labeled a. c. The time the gas mixture was tolerated after meals is represented in the right hand column, marked p. c.

ciable increase in coronary flow within the time limits of these experiments.

The effect of the ingestion of food in varying times up to twenty minutes following the meal is shown in table 3. The occurrence of anginal pain following meals has been explained by many writers as due to the inability of the anatomically damaged vessels to meet this demand and that the anatomic damage was the only factor involved. While this is true in many cases, we believe that in many other cases increased vagal tone, or a vasovagal reflex, as described by Weiss and others, plays an important part in the production of pain. Atropine has long been mentioned as an instrument to increase the coronary flow, but no one has been impressed with the significance of this observation. Essex and his co-workers¹⁸ comment on this in a recent

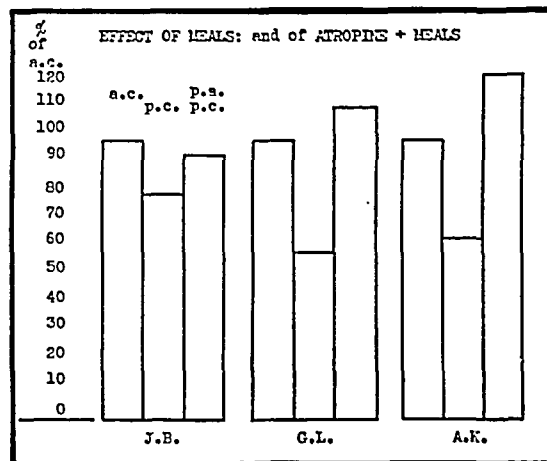


Chart 2.—The tolerance for 10 per cent oxygen before meals is represented in the left hand column of each group as 100 per cent and is labeled a. c. The tolerance for the gas mixture after meals is depicted in the middle column, labeled p. c. The right hand column represents the tolerance after atropine, after meals, and is marked p. a. p. c.

almost no difference. There was actually a reduction of 3.7 per cent in the pain time after atropine. Reference to table 2 will show that patient 1 was a 70 year old man with hypertension and cardiac enlargement. From the physical examination alone, one would suspect the presence of considerable anatomic change in the heart. This, together with the atropine response shown in chart 4, would indicate that the vagal tone was not as important a factor in the production of pain as with patient 2, whose pain time after atropine was increased

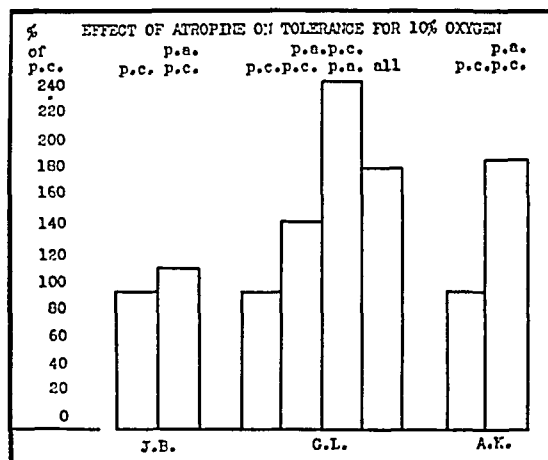


Chart 3.—The tolerance for 10 per cent oxygen after meals is represented as 100 per cent in the left hand one of each group of columns and is labeled p. c. The group of columns with the subscript G. L. represents the following: p. c., tolerance after meals = 100 per cent; p. a. p. c., atropine was given, the meal was eaten and then the test was run; p. c. p. a., the meal was eaten, atropine was given and then the test was run; all the tolerance for 10 per cent oxygen after meals and atropine regardless of the time when the drug was given.

33 per cent. Patient 2 had a very slight elevation of pressure and a normal sized heart, and from the physical examination alone it would be difficult to detect cardiac structural changes. With these data in mind, one

18. Essex, H. E.; Herrick, J. F.; Baldes, Edward J., and Mann, F. C.: Blood Flow in the Circumflex Branch of the Left Coronary Artery in the Intact Dog, *Am. J. Physiol.* 117: 271-279 (Oct.) 1936. Essex, H. E.; Wegria, R. G. E.; Herrick, J. F., and Mann, F. C.: The Effect of Certain Drugs on the Coronary Blood Flow of Trained Dogs, *Am. Heart J.* 19: 554-565 (May) 1940.

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would suspect a much greater vasoconstrictor element in the anginal attacks of patient 2 and a greater organic element in the anginal attacks of patient 1. If this were true, one would forecast the more profound effect that the ingestion of food would have on patient 2 and a greater response from atropine after a meal. That this

We do not need to be convinced that the xanthine bodies increase the coronary flow. Our belief in the efficiency of theobromine and theophylline has been a matter of record for several years. In addition to this, Levy¹⁷ and his associates have already used this method to show the increase in pain time caused by the administration of these drugs. In order to compare the effect of atropine and theophylline on the same patient under the same conditions, an additional experiment was done.

We show in chart 5 that a result in the same direction may be obtained in the first instance by a vagal inhibitor and in the second instance by a coronary vasodilator. As might be expected, the active coronary vasodilator had the more marked effect. The result shown in chart 5 was the effect of a single injection of 0.5 Gm. of theophylline with ethylene diamine. When this patient had taken orally 0.6 Gm. of the drug daily for three days it was impossible to produce pain by the respiration of 10 per cent oxygen for thirteen minutes longer than the control pain time.

COMMENT

Our experiments would seem to indicate quite definitely that the coronary flow in the dog may be reduced by distention of the stomach or abdominal cavity. The results are quite constant if proper attention is paid to anesthesia and the dog is maintained in relatively good condition. In view of the fact that this reduction in flow does not occur after vagal section or after the administration of atropine, it is difficult to escape the conclusion that the reduction in flow is the result of activity of the vagus nerve. This, then, is an instance of reflex coronary vasoconstriction initiated by vagal irritation in the gastrointestinal tract. Attention has been directed to the results of other workers who have brought out evidence indicating the occurrence of a similar reflex coronary vasoconstriction initiated in the lung¹⁰ and in the heart itself.⁹ We feel that similar effects may result from irritation of the gallbladder or biliary tract, and we hope to report later on further experimental work. It would seem quite likely that such vasoconstrictor reflexes might also originate elsewhere in the viscera, but definite proof is lacking. If it is assumed that reflex coronary vasoconstriction may be the result of gastric or abdominal distention, the incidence of anginal pain following meals is explained in part.

In an effort to examine this hypothesis with patients having angina of effort, such patients were subjected to a pain-stimulating mechanism. They were made to breathe 10 per cent oxygen until the pain appeared and it was found that the time required to produce pain in a given patient was remarkably constant from test to test. This induced pain appeared much more quickly following meals, and this reduced pain time was abolished by the use of atropine. In the clinical patient the anginal attacks appear more promptly after ingestion of food. In the experimental animal, distention of the stomach was followed by a decrease in the coronary flow. In each case the effect was abolished by atropine. In the experimental animal the effect did not occur after section of the vagus.

In examining the individual patients by the method described, a fairly wide variation in the response to atropine was observed. It seemed to us that the variation of the pain time in response to atropine was in inverse proportion to the evidence of anatomic cardiac

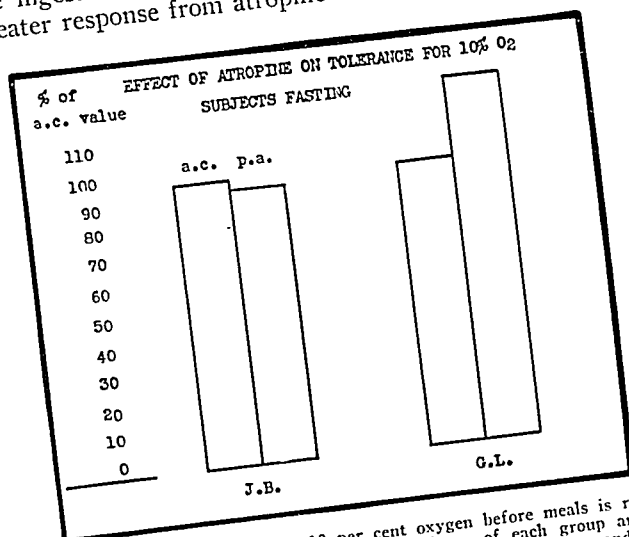


Chart 4.—The tolerance for 10 per cent oxygen before meals is represented as 100 per cent in the left hand column of each group and is labeled a. c. The tolerance for the gas mixture after atropine, and still before meals, is represented in the right hand column, labeled p. a.

was the fact was shown in table 4. The ingestion of food reduced the tolerance to 10 per cent oxygen of patient 1 by 19 per cent, of patient 2 by 40 per cent. Atropine improved the after meal tolerance for 10 per cent oxygen of patient 1 by 17 per cent, of patient 2 by 87 per cent. The remaining figures in table 4 are those from which the graphs were prepared.

In January of this year, while the work was in progress, Morrison and Swalm¹⁹ published a report in which

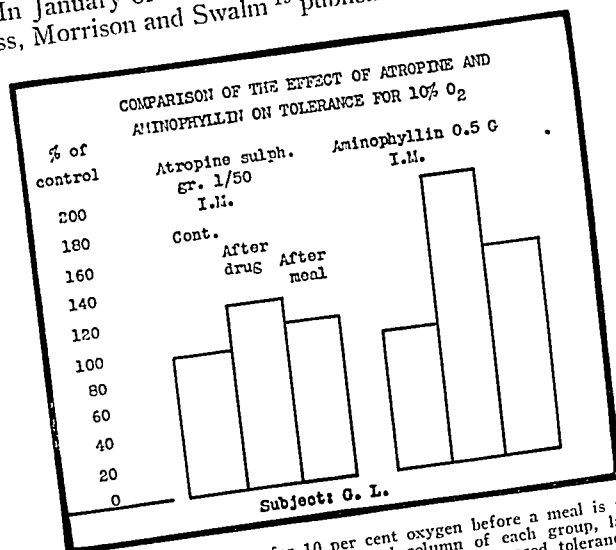


Chart 5.—The tolerance for 10 per cent oxygen before a meal is represented as 100 per cent in the left hand column of each group, labeled Cont. (control). The middle column depicts the increased tolerance for the gas twenty minutes after each drug was given. The right hand column represents the tolerance to the gas ten minutes after completion of a meal that was served immediately after the test represented in the middle column.

they approached this problem from a somewhat different angle, and we believe that our results are in every way consistent with theirs.

19. Morrison, L. M., and Swalm, W. A.: Role of the Gastrointestinal Tract in Production of Cardiac Symptoms, J. A. M. A. 114:217-223 (Jan. 20) 1940.

damage. That is to say, the greater the obvious cardiac damage, the less striking is the atropine response. It is probable that the ability of a seriously damaged coronary vessel to dilate or constrict is impaired. We think that this observation indicates a vasoconstriction in the cases in which atropine gave relief. It is quite possible that the character of the atropine response by such patients may be a rough index of the character of the angina. A considerable increase in the tolerance to 10 per cent oxygen as a result of the injection of atropine by patients subjected to this procedure would lead us to suspect that the anginal attack had a large vasoconstrictor element. Conversely, a small atropine response would indicate that the angina was largely due to anatomic changes in the vessel.

CONCLUSIONS

Distention of the dog's stomach under light anesthesia or no anesthesia at all produces coronary vasoconstriction through a vagovagal reflex. This reflex with its resultant coronary constriction may be abolished by atropine or by vagal section.

Anginous patients who were made to breathe 10 per cent oxygen developed anginal pain much more quickly following meals. This reduced pain time was abolished by the use of atropine and, in two of the three patients, atropine caused the after meal pain time to exceed the control pain time.

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ABSTRACT OF DISCUSSION

DR. LESTER M. MORRISON, Philadelphia: Drs. Gilbert, Fenn and LeRoy have shown the relationship of intragastric gassy distention on the coronary arteries. It is gratifying to find their work in complete agreement with my experimental and clinical studies reported in *THE JOURNAL*, January 20. At that time Dr. Swalm and I recorded the effect and relationship of intragastric and intra-esophageal gassy distention on the coronary arteries and angina pectoris in man for the first time and showed their direct relationship clinically through the vagus arc. When we first conducted our experiments in 1935 it took Dr. Peckham and myself some six months to devise a safe apparatus, because of the danger of inducing a fatal attack in the cardiac cases. Indeed, when I distended the stomach to 100 mm. of mercury pressure one of the patients developed a cardiac standstill and fell unconscious. If we had not constructed our apparatus so that I could relieve the intragastric pressure immediately, I feel certain that the patient would have died then and there. It is a tribute to the skill and ingenuity of Drs. Gilbert, Fenn and LeRoy that their method of approach was so eminently successful. The variability of the time-pain in each of the cases presented indicates the difference in vagal pattern sensitivity in different patients. This calls for saturation dosages of atropine or belladonna for therapeutic effectiveness. Dr. Fenn told me that the experimental meals were given at the lunch hour. Even more striking results may have been obtained following the heavy evening meal, which is a much heavier load placed on the stomach and the vagus nerve mechanism. The clinical inferences of this presentation are significant. In angina pectoris and coronary artery disturbances the necessity is for small, frequent meals, proper diet, antispasmodics, sedatives and xanthine derivatives. The diet should be relatively bland, easily digested and free from all gas-forming foods. Light meals should always be eaten slowly and chewed thoroughly. Active physical exercise or excitement after meals is always hazardous in these cases and is to be avoided at all times. The bowels should function normally and daily. Flatulence is to be avoided like the plague and can be combated with soothing gastric and bowel demulcents, antacid powders, carminatives and absorbents.

DR. CHARLES W. GREENE, Stanford University, Calif.: It is reassuring to find that clinicians are laying more and more emphasis on the part played by physiologic processes in the origin and course of cardiac disorders. The foundation of the nutritive control of the myocardium lies in intimate regulation of the coronary blood flow. It is the details of this regulation that are being uncovered by the numerous coronary researches of the last two decades. Sensory events in every part of the body produce autonomic reflexes directly affecting the rate and volume of the coronary blood flow. It matters not what associated reactions may simultaneously occur. Dr. Gilbert and his colleagues have added the demonstration of the part played by visceral pressure stimulation. A fact not generally known is that the milder and usual functional coronary reflexes take the form of coronary dilatations. Reflex coronary constrictions occur in the normal animal only in response to more vigorous sensory stimulation. If, as is often the case, the constrictor reflex apparatus is hypersensitive or overdeveloped, coronary constrictions are more frequent, even dominant, and may be profound enough to induce varying degrees of myocardial ischemia. The authors have used the two reliable and standard experimental methods applicable to dogs, the coronary sinus method and the electrical stromuhr technic. Each method is difficult but each yields data which supplement the other. The addition of direct experiments on anginal patients is unique. The method arrives at the cardiac crisis sooner. The reported results are positive and definite. Let me emphasize that reflex coronary reactions are almost always associated with cardiac accelerations, not slowing or inhibitions as is too often inferred. This is the explanation of the coronary dilatation as the normal and standard reaction. The coronary dilatation supplies more oxygen when the myocardial consumption is greater. One can appreciate the upset of this physiologic balance when the coronary arteries are reflexly constricted, thus actively reducing the coronary flow. It is equally tragic if the coronaries of the patient are sclerotic or have lost coronary resilience and cannot respond to the associated coronary dilator reflexes when the heart is doing increased work. The authors are to be congratulated for establishing that visceral pressures induce reflex coronary constrictions that hasten anginal attacks.

DR. HEYMAN R. MILLER, New York: These studies touch on two major problems: The first deals with the question Does anoxemia with a resultant myocardial ischemia produce anginal pain? Does anginal pain associated with abdominal distention depend on anoxemia? The other major problem is unrelated to anoxemia and has to do with the transmission of afferent impulses from the abdomen and its viscera to those spinal cord segments at which referred cardiac pain is mediated. Afferent abdominal stimuli are probably also registered in the cardiac apparatus by means of axon reflexes, without passing through the spinal cord. May I ask whether it is not possible to have an anoxemia, a diminished oxygen content in the circulation, and yet an oxygen content in the heart muscle above the critical level requisite for the induction of pain? I put the question because the heart with its special arrangement of autonomic supplies seems able to receive more rather than less blood in the presence of an emergency like asphyxia; the coronary vessels probably dilate. Moreover, in certain experimental and clinical situations the heart, despite low oxygen content of the blood, can remain free of pain. While intense pain will appear at the moment of tightening a ligature around a coronary vessel, shortly thereafter, and despite continued anoxemia of the heart muscle, pain may subside or disappear. Again, at the onset of an acute coronary thrombosis, pain is often intense yet within a few hours cardiac pain may be greatly diminished or absent even though the infarcted segment of myocardium is still deprived of considerable oxygen. These observations are offered not as complete detractors of the general concept that anoxemia may lead to cardiac pain but rather to suggest that factors other than anoxemia alone are at work. The observations of Dr. Greene and his co-workers indicate that a reflex may operate between abdominal viscera and the coronary circulation. I venture to believe, however, that such a reflex may influence coronary flow independent of the mechanism of pain transmission.

THE TREATMENT OF ANURIA DUE
TO SULFAPYRIDINE CALCULI

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The symptom complex of hematuria, abdominal pain, and nitrogen retention as a manifestation of sulfapyridine therapy was first described by Southworth and Cooke,¹ although the occurrence of hematuria had been previously noted.²

Animal experiments by Antopol and Robinson,³ Gross, Cooper and Lewis⁴ and Toomey⁵ early revealed the pathologic changes in the urinary tract of rats, rabbits and monkeys receiving sulfapyridine. Since then, Antopol and Robinson⁶ and Toomey, Reichle and Takacs⁷ have studied these changes in great detail. Briefly they are as follows: in the kidneys, striking dilatation of the glomerular spaces and tubules; thickening of the basement membranes of the glomerular tufts with changes in the shape of the cells of the capsular epithelium; in the collecting tubules, debris and spaces, apparently the lodging place of crystals of the precipitated drug; in the pelvis and ureters, concretions, with denuding of the epithelium, clotted blood, mucosal hemorrhages and marked edema.

The seriousness of this manifestation of sulfapyridine treatment in man became evident with the report of a death from total anuria by Tsao and his co-workers.⁸ This report was of particular interest in that the finding of complete ureteral obstruction due to concretions blocking both ureterovesical orifices was described. These authors suggested the use of cystoscopic treatment, believing that their patient would have survived if this procedure had been carried out.

Recently Carroll, Shea and Pike⁹ have successfully treated by cystoscopy a patient who had complete anuria due to sulfapyridine calculi and have recorded the finding of ureteral obstruction by calculi at the ureterovesical orifices.

Our purpose in the present contribution is to offer additional evidence (1) that complete anuria due to

sulfapyridine may be caused by ureteral obstruction and (2) that this condition can be treated effectively by means of cystoscopy. The renal pathologic changes in one instance of acute sulfapyridine anuria will be described.

REPORT OF CASES

CASE 1.—History.—A man aged 35, Italian, a laborer, was admitted on Feb. 3, 1940, to the Neurosurgical Service of the New Haven Hospital following a traumatic injury to the head with penetration of a foreign body into the right frontal region of the brain. Little was known of his past history other than that he had enjoyed good health up to the time of the accident.

On admission the patient was unconscious, breathed stertorously and did not respond to stimuli. The temperature was 100.2 F., pulse 88 and respiratory rate 48. The blood pressure was 190 systolic, 120 diastolic but shortly after admission fell to 110 systolic, 80 diastolic. Examination revealed a deep laceration of the right frontal region in which was embedded a foreign object. Shortly after admission the patient



Fig. 1 (case 1).—Retrograde pyelogram before lavage of kidney pelvis.

fell into shock but after operative removal of the foreign body and blood transfusion he rallied and his condition seemed quite satisfactory.

Following operation the administration of sulfapyridine was commenced as a prophylactic measure but, despite this, infection of the operative wound set in within forty-eight hours and cultures of the pus yielded a growth of hemolytic *Staphylococcus albus* and *aureus*. Essential details of the patient's course are outlined in table 1. On the first day he received 3 Gm. of sulfapyridine, the first 2 Gm. of which was administered subcutaneously in 750 cc. of saline solution and 750 cc. of 5 per cent dextrose. All subsequent sulfapyridine was given by mouth in the amount of 1 Gm. every four hours until February 6. On this date because of a rather low blood level of free sulfapyridine the dosage was increased to 1 Gm. every three hours.

At noon on February 7 the patient complained of pain in the flanks. That night the urine was found to be of a dark amber color and to contain about 25 red cells per high power field in an uncentrifuged specimen. Sulfapyridine was immediately discontinued and fluids were forced as much as possible under the circumstances of the accompanying neurologic condition.

From the Departments of Internal Medicine, Pathology and Surgery of the Yale University School of Medicine and the New Haven Hospital.
1. Southworth, Hamilton, and Cooke, Crispin: Hematuria, Abdominal Pain and Nitrogen Retention Associated with Sulfapyridine, *J. A. M. A.* **112**: 1820 (May 6) 1939.

2. Lawrence, E. A.: Recent Advances in the Treatment of Pneumonia, *International Review of Recent Advances in Medicine* **3**: 45 (Jan.) 1939.
Hanssen, Per: Treatment of Lobar Pneumonia, *Brit. M. J.* **693**, *Lancet* **1**: 61 (Jan. 7) 1939. Graham, J. W., and Dauphinee, J. A., and Dickson, R. C.: The Pathology of Pneumonia with Dagenan (M. & B. 693), *C. M. A. J.* **10**: 337 (April) 1939.

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5. Toomey, J. A.: Urinary Concretions and Sulfapyridine, *J. A. M. A.* **113**: 250 (July 15) 1939.

6. Antopol, William, and Robinson, Harry: Pathologic and Histologic Changes Following Oral Administration of Sulfapyridine, with a Short Note on Sulfapyridine, *Arch. Path.* **29**: 67 (Jan.) 1940.

7. Toomey, J. A.; Reichle, H. S., and Takacs, W. S.: Effects on Monkeys of Sulfapyridine in Doses Comparable with Those Used for Humans, *J. Pediatr.* **16**: 179 (Feb.) 1940.

8. Tsao, Y. F.; McCracken, Mary E.; Chen, Ji; Kuo, P. T., and Dale, C. L.: Renal Complications in Sulfapyridine Therapy, *J. A. M. A.* **113**: 1316 (Sept. 30) 1939.

9. Carroll, Grayson; Shea, John, and Pike, George: Complete Anuria Due to Crystalline Concretions Following the Use of Sulfapyridine in Pneumonia, *J. A. M. A.* **114**: 411 (Feb. 3) 1940.

The following day the patient was irritable but responded well to stimuli. Respirations were rapid. The left retinal fundus was normal in appearance. The lungs were clear throughout, and examination of the cardiovascular system revealed no abnormalities. The abdomen was greatly distended and tym-



Fig. 2 (case 1).—Retrograde pyelogram after lavage of kidney pelves.

panic. Palpation over both costovertebral angles showed definite tenderness. There was no peripheral edema. Little fluid had been taken by mouth. Consequently fluids were given parenterally in a total amount of 3,100 cc. as follows: 300 cc. transfusion of blood, 1,000 cc. of 10 per cent dextrose solution and 300 cc. of physiologic solution of sodium chloride intra-

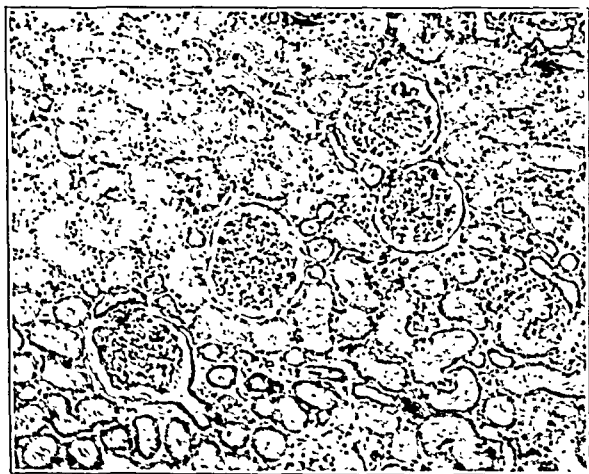


Fig. 3 (case 1).—Section of renal cortex showing dilatation of tubules and glomerular spaces. Reduced from a photomicrograph with a magnification of 100 diameters.

venously, and 1,000 cc. of physiologic solution of sodium chloride and 500 cc. of 5 per cent dextrose solution by hypodermoclysis.

During the remainder of the day the patient complained rather bitterly of persistent pain in the flanks and difficulty in voiding. At 4:30 p. m. he passed 60 cc. of grossly bloody urine, his last voided specimen.

Following this there was complete anuria during the next twenty-four hours, despite intravenous injection of physiologic solution of sodium chloride and 50 per cent dextrose. The possibility of sulfapyridine calculi blocking the ureters was considered and it was decided that cystoscopy was indicated, since the patient's nonprotein nitrogen was now 76 mg. per hundred cubic centimeters.

A No. 24 French cystoscope was passed with ease. Approximately 50 cc. of pinkish cloudy amber urine was found in the bladder and showed the characteristics detailed in table 2. In it were many long slender crystals and large flat ones which were jagged and irregular. The bladder capacity was less than 100 cc. The mucous membrane was injected and a few small blood clots were present. The ureteral orifices were inflamed and a small blood clot was seen protruding from the left meatus. Neither ureteral orifice passed any urine. Attempts to pass the ureteral catheters met obstruction on both sides at a depth of 1 cm. The catheters were then withdrawn and after the passage of No. 5 filiform tipped bougies, No. 7 French ureteral bougies were passed to the renal pelvis on both sides. Following withdrawal of these, a sharp, multipointed concretion was seen extruding from the right ureteral orifice. This was easily dislodged. Each ureteral orifice was now seen to produce bloody urine and on catheterization yielded urine as described in table 2.



Fig. 4 (case 1).—Section of renal pelvis showing the loss of epithelium and the massive hemorrhagic infiltration of the lamina propria mucosae. Note also the congestion of the submucosal vessels and the cellular infiltration of this layer. Reduced from a photomicrograph with magnification of 40 diameters.

An x-ray film of the abdomen was rather unsatisfactory because of intestinal distention, but no evidence of radiopaque renal or ureteral calculi was found. A retrograde pyelogram (fig. 1) revealed poorly outlined renal pelves with mottling and hazy outlines. Both catheters were now repeatedly washed out with warm sterile water for a period of about thirty-five minutes. At the end of this period the urine draining from the left catheter was fairly clear while that draining from the right catheter remained blood tinged. A retrograde pyelogram (fig. 2) now revealed more sharply outlined kidney pelves. The ureteral catheters were allowed to remain in place, the left producing from 50 to 60 drops a minute and the right from 30 to 40 drops a minute.

The patient was then returned to the ward and during the next two hours continued to excrete urine satisfactorily from both catheters, at the end of which time he pulled the catheters out of place. Shortly after this, 1,000 cc. of 5 per cent dextrose solution was given slowly by the intravenous route. Approximately thirty minutes after the infusion was finished the patient lapsed into coma and, despite supportive measures, died of respiratory failure, presumably due to cerebral edema and medullary compression.

Pathologic Examination.—Autopsy was limited to an examination of the kidneys and the upper portions of the ureters. Grossly the kidneys were enlarged, the right weighing 230 Gm. and the left 215 Gm. The measurements for the right were 12 by 7 by 5 cm. and for the left 12 by 6 by 4.5 cm. Both

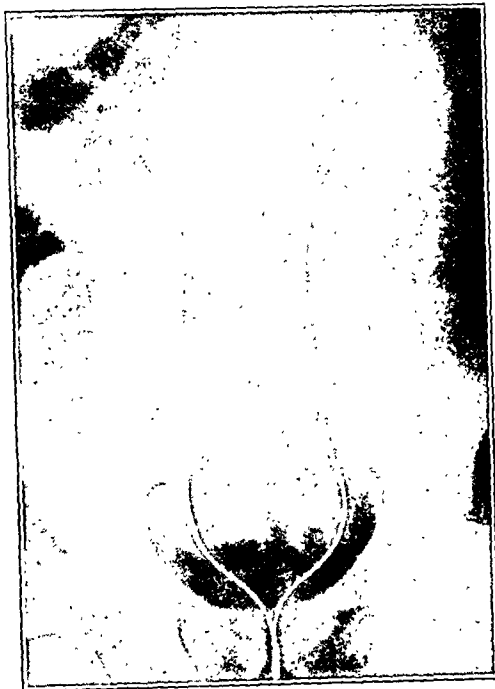


Fig. 5 (case 2).—Retrograde pyelogram before lavage of kidney pelvises.

organs were light brown and quite soft. Their capsules stripped with ease, leaving a smooth surface on which there was no evidence of potential hemorrhages. On longitudinal section the



Fig. 6 (case 2).—Retrograde pyelogram after lavage of kidney pelvises.

cut edge of the renal tissue bulged slightly, denoting increased tension. The cortical and medullary markings of the parenchyma were distinct, the cortex measuring from 6 to 8 mm. in diameter. No gross hemorrhages could be identified on the cut surface. There was no dilatation of the renal pelvises or ureters but the mucosal surfaces of these structures were markedly altered

in appearance. Much red-brown clotted blood, rather granular in consistency, filled the calices and was adherent to large areas of the pelvic and ureteral mucosa. Where there was no actual clot the pelvis and ureteral mucosal surfaces were hemorrhagic, being raised here and there into small bleblike masses filled with blood. The walls of the pelvises and ureters were markedly edematous. No concretions were present, but in the calices, mixed with the clotted blood, were found small amorphous masses of a light red-brown material which was gritty to palpation. Under the microscope numerous needle shaped and sheaflike crystals were identified. Chemical analysis¹⁰ of this material revealed the presence of 45 per cent acetylated sulfapyridine and 6 per cent free sulfapyridine.

Microscopically the most striking change in the kidney proper was the great dilatation of the convoluted and collecting tubules and of the glomerular spaces. A considerable amount of eosinophilic granular material was observed in the convoluted tubules. In a few of the collecting tubules, basophilic amorphous masses were found but no other concretions or crystals were present. The glomerular changes were interesting. In addition to the distention of Bowman's capsule the tufts were enlarged with greatly congested capillaries and a much vacuolated intercapillary basement membrane. In numerous tufts the red blood cells within the capillaries were apparently fused or conglu-

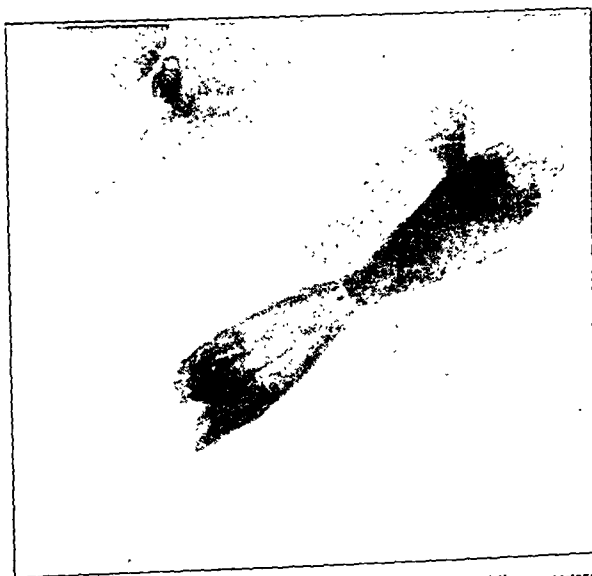


Fig. 7 (case 2).—Sheaf of crystals of acetyl sulfapyridine recovered from the ureteral calculi; $\times 200$.

minated to form homogenous eosinophilic masses. Neither necroses of the glomerular tufts nor intracapsular hemorrhages were found. The epithelium of the renal tubules was intact throughout. Focal areas of capillary congestion were frequent and there was much interstitial edema.

The renal pelvises showed for the most part absence or necrosis of their transitional epithelium. The lamina propria mucosae was edematous and contained large hemorrhagic extravasations, some of which resulted in the nodular masses noted grossly. Numerous lymphocytes and polymorphonuclear leukocytes were present. Similar hemorrhagic extravasations and cellular accumulations extended in focal zones through the submucosa well up into the medullary renal tissue.

Microscopically the ureters showed extensive mucosal hemorrhages, great edema of all the coats of the wall and an abundant lymphocytic and polymorphonuclear cellular infiltration.

CASE 2.—A man aged 39, Italian, a laborer, was first admitted for therapy to the Medical Service of the New Haven Hospital on Dec. 11, 1939, with a subacute gonorrheal urethritis, prostatitis and arthritis. Some degree of improvement occurred on sulfanilamide therapy, but the patient left the hospital against advice on Dec. 26, 1939.

10. Chemical analyses in this report were performed by Miss Anne Seymour.

Eight days after discharge the patient again had a urethral discharge, which was shortly followed by pain and swelling of both ankles and the right knee. He was readmitted on Feb. 7, 1940, with an arthritis of both ankles and the right knee, the latter being quickly followed by spread to the left knee. His temperature was 102 F. and blood pressure 120 systolic, 80 diastolic. The leukocyte count was 11,300. Examination of the urine revealed no albumin or red cells, but from 1 to 2 leukocytes per high power field were present. X-ray examination of the ankles and right knee revealed changes consistent with a subacute infectious arthritis.

After a preliminary period of observation, sulfathiazole therapy was begun, the patient receiving an initial dose of 4 Gm. followed by 1 Gm. every four hours. No response in temperature or symptoms was obtained and after six days of therapy sulfathiazole was discontinued. Specific details as to the laboratory data are contained in table 4.

Twenty-four hours after the discontinuance of sulfathiazole the blood concentration of the drug had fallen to a trace, and eight hours after this determination sulfapyridine therapy was begun, the patient receiving an initial dose of 4 Gm. and then 1 Gm. every four hours. On the third day of sulfapyridine therapy (February 19) it was noted that 55 per cent of the drug in the blood was acetylated, but in view of a normal urine, a nonprotein nitrogen of 27 and a satisfactory urine output it seemed advisable to continue sulfapyridine therapy. Late that night the patient complained of lower abdominal pain but nothing was found on physical examination except abdominal distention.

TABLE 1.—Data in Case 1

Date	Sulfapyridine Admin. Gm.	Fluid Intake, Cc.	Urinary Output, Cc.	Sulfapyridine Blood Concentration			Non-protein Nitrogen, Mg. %	CO ₂ , Vol. %	Chloride, mEq.
				Free, Mg. %	Total, Mg. %	Acetylated, %			
Feb. 3	3.0	1,500	400
4	6.0	2,000	600
5	6.0	2,000	650	2.4
6	8.0	960	350	3.3
7	6.0	4,200	425	3.1
8	...	4,100	135	70	49.0	99.4	...
9	...	2,800	0	2.2	15.2	85	76	44.9	97.0

Intake and output levels on twenty-four hour specimen from 7 a. m. to 7 a. m. The fluid intake includes fluids given parenterally.

At 4 o'clock the following morning (February 20) the patient passed a dark smoky urine containing innumerable red cells, 3 plus albumin and numerous crystals, among which were a type resembling bound sheaves of wheat. This specimen contained 92.4 mg. per hundred cubic centimeters of free sulfapyridine and 235 mg. total sulfapyridine (61 per cent acetylated). From this point on the patient had an essentially complete anuria and now complained of rather severe pain definitely localized over the suprapubic area and the costovertebral angles. The nonprotein nitrogen had risen to 35 mg. per hundred cubic centimeters and total blood sulfapyridine to 13.7 mg., 57 per cent of which was acetylated. There was a leukocytosis of 22,200, 85 per cent of the cells being of the granulocytic series.

Sulfapyridine was immediately discontinued and fluid forced both orally and parenterally, the patient receiving 1,000 cc. of 10 per cent dextrose intravenously and 3,250 cc. of physiologic solution of sodium chloride and 750 cc. of 5 per cent dextrose by hypodermoclysis. During the course of the day the patient complained bitterly of pain in the flanks and lower part of the abdomen. There was costovertebral tenderness, more marked on the right.

Except for 5 cc. of bloody urine passed at 5 a. m. February 21, which had essentially the same characteristics as the last specimen passed on February 20, no further urine was produced. By the morning of February 21 he had become drowsy and lethargic. The nonprotein nitrogen had risen to 45 mg. per hundred cubic centimeters and the total blood sulfapyridine to 15 mg., 67 per cent of which was in the acetylated form. At 3:30 that afternoon, after anuria for thirty-six hours, cystoscopy was performed.

A No. 24 French cystoscope was passed without difficulty, a slightly grating sensation being noted. About 20 cc. of grossly

bloody urine was found in the bladder. The bladder capacity was 200 cc. The bladder mucous membrane was fairly normal except for moderate inflammation in the region of the trigon. There were numerous mucous shreds and yellowish concretions in the base of the bladder. Neither ureteral orifice produced

TABLE 2.—Characteristics of Urine from Bladder, Right Ureteral Catheter and Left Ureteral Catheter Obtained at Cystoscopy in Case 1

	Bladder	Right Kidney	Left Kidney
Appearance.....	Pinkish, cloudy amber	Grossly bloody	Cloudy amber
Reaction.....	Acid	Acid	Acid
Albumin.....	+	+++	+
Sediment (centrifuged)			
Red blood cells.....	Innumerable	Innumerable	50 per high power field
White blood cells.....	Occasional	None	None
Casts.....	None	None	None
Epithelial cells.....	Moderate number	None	None
Sulfapyridine concentration			
Free.....	70 mg. per 100 cc.	65 mg. per 100 cc.	90 mg. per 100 cc.
Total.....	355 mg. per 100 cc.	265 mg. per 100 cc.	395 mg. per 100 cc.
Acetylation.....	78 per cent	76 per cent	77 per cent
Culture.....	Sterile		

any urine. The right ureteral orifice was swollen, edematous and dusky red, and humped up on a mount about 1 cm. in diameter. Protruding from the ureteral orifice could be seen a large irregular concretion completely filling the meatus. The left ureteral orifice was similarly involved but less edematous and was also completely filled with a calculus. No. 5 French ureteral catheters were then passed. There was moderate obstruction for a distance of about 2 cm. from the meatus. Beyond this point they passed without difficulty to the renal pelves, urine dropping from the left ureteral catheter quite steadily, but more slowly on the right. The right ureteral catheter was then withdrawn momentarily and a most remarkable sight was seen. Pouring from the right ureteral orifice was a thick sludge, probably sulfapyridine "sand," quite similar in appearance to the pouring of a thick semisolid cement mixture. After this material was discharged the catheter was reinserted and ureteral specimens were taken for examinations which are summarized in table 3. An x-ray film of the abdomen revealed no radiopaque calculi present. A retrograde pyelogram (fig. 5) revealed a dilatation of the right ureter. The renal pelves were fairly normal though rather mottled in appearance,

TABLE 3.—Characteristics of Urine from Bladder, Right Ureteral Catheter and Left Ureteral Catheter Obtained at Cystoscopy in Case 2

	Bladder	Right Kidney	Left Kidney
Appearance.....	Grossly bloody	Blood tinged	Cloudy amber
Reaction.....	Neutral	Acid	Acid
Albumin.....	+++	+	Trace
Sediment (centrifuged)			
R. B. C.....	Innumerable	Innumerable	100 per h. p. f.
W. B. C.....	25 per h. p. f.	Occasional	Occasional
Casts.....	None	None	None
Sulfapyridine Conc.			
Free.....	80.0 mg. per 100 cc.	47.5 mg. per 100 cc.	
Total.....	210.0 mg. per 100 cc.	145.0 mg. per 100 cc.	
Acetylation.....	62%		67%
Culture.....	Sterile		Sterile

this being especially true of the right kidney pelvis. The catheters were then thoroughly lavaged with warm distilled water and the pyelogram was repeated (fig. 6), showing better filled pelves with clearer outlines.

Phenolsulfonphthalein was injected intravenously, appearance times of the drug being four and one-half and three minutes respectively on the left and right sides. Excretion on the left side in fifteen minutes was 2.5 per cent, while on the right side

it was approximately 10 per cent, the latter figure being unreliable owing to the presence of blood. A number of small stones were then washed out of the bladder and preserved. They were yellowish white, irregularly spherical and easily crushed. Microscopically they were made up for the most part of groups of crystals resembling bound sheaves of wheat (fig. 7) together with a number of long slender needles (probably from the breaking up of the sheaves) and crystals of nonacetylated sulfapyridine. Chemical analysis of these calculi showed that they contained 55 per cent of acetylated sulfapyridine and 7 per cent of free sulfapyridine.

The ureteral catheters were allowed to remain in place for the next twelve hours. Urine dropped steadily from each ureteral catheter, and from time to time the patient voided spontaneously around the catheters. During this period the left catheter yielded 255 cc. of urine containing 35 mg. per hundred cubic centimeters of free sulfapyridine and 110 mg. of total sulfapyridine (68 per cent acetylation), the right catheter 370 cc. of urine containing 37.5 mg. per hundred cubic centimeters of free sulfapyridine and 115 mg. of total sulfapyridine (67 per cent acetylation).

Following removal of the catheters the patient continued to pass considerable quantities of a dark smoky urine containing

McLellan.¹¹ Under these circumstances treatment of sulfapyridine hematuria by means of forced fluids alone seems ample, since data¹² have been offered to suggest that the concretions may be redissolved or washed out.

If, however, complete anuria is present or if the possibility of a unilateral obstruction is evident, cystoscopy should be done without delay to determine whether or not urine is being passed from the ureteral orifices. If not, catheterization of the ureter, a filiform tipped bougie being used if necessary, should be carried out and the kidney pelvis and ureter thoroughly lavaged with warm distilled water until the urine drips from the catheter and retrograde pyelograms reveal a clearly outlined upper urinary tract.

It is perhaps preferable to leave the ureteral catheters in place for the next twelve hours, though this may not be absolutely necessary. From time to time the catheters should be irrigated with warm saline solution and after their withdrawal fluids should be continually

TABLE 4.—Data in Case 2

Date	Dosage of Sulfathiazole, Gm.	Dosage of Sulfapyridine, Gm.	Fluid Intake 24 Hr., Ce.	Urinary Output, Ce.	Leukocytes in Blood	Sulfathiazole Blood Concentration			Sulfapyridine Blood Concentration			Non-protein Nitrogen, Mg. per 100 Ce.	Urine			
						Free, Mg. per 100 Ce.	Total, Mg. per 100 Ce.	Acetylation, %	Free, Mg. per 100 Ce.	Total, Mg. per 100 Ce.	Acetylation, %		Albu- min	R. B. C. per H. P. F.	C. W. B. C. per H. P. F.	W. B. C. per H. P. F.
Feb. 10	6.0	9,600
11	6.0	9,500	0	0
12	6.0	10,100	2.9	3.8	23	0	0
13	6.0	...	2,800	1,250	10,200	3.8	4.5	16	0	0
14	6.0	...	3,700	1,550	12,200	3.1	3.6	14	28	0	0
15	6.0	...	3,300	1,900	7,700	3.1	4.0	23	0	0
16	1.0	...	3,200	1,760	7,400	2.0	3.5	26	0	0
17	...	7.0	3,770	3,000	8,800	tr.	tr.	0	0
18	...	6.0	3,100	1,750	7,800	0	0
19	...	6.0	3,050	2,650	7,100	3.2	7.2	55	27	0	0
20	...	1.0	6,000	5	22,200	5.9	13.7	57	35	+++	100	5	...
21	2,450	939	18,700	4.9	15.0	67	45	++	100	5	...
22	2,700	2,195	12,300	1.9	7.4	74	...	+	10	5	...
23	4,450	2,420	10,600	0.7	3.8	82	39	0	rare	3	...
24	3,100	2,450	15,800	tr.	1.0	...	39
25	5,770	1,550	tr.	tr.
26	2,850	1,275	12,000	34
27	4,050	1,100	0	rare	rare	...
28	3,945	1,650	30

Intake and output levels on twenty-four hour specimens from 7 a. m. to 7 a. m. The fluid intake includes fluids given parenterally. Medication charted for twenty-four hours, 4 a. m. to 4 a. m.

red cells, albumin, mucous shreds and many very small calculi, which on microscopic examination showed again the presence of large jagged crystals, apparently broken up acetylated sulfapyridine crystals. He continued to pass similar urine until the night of February 22, following which the urine assumed a slightly cloudy, yellow appearance. The urine continued to clear, the albumin disappeared and only rare red and white cells were found. At the time of discharge the urine was entirely negative save for an occasional leukocyte. Casts were never found in the urine at any time. Phenolsulfonphthalein excretion on February 26 was 63 per cent in two hours. An intravenous pyelogram revealed normal kidney pelvis and normal ureters, the dilatation of the right ureter previously observed being no longer present.

The patient was discharged on March 12, 1940, in good condition with temperature normal, arthritis practically subsided and normal urinary status.

COMMENT

In both cases there remains no doubt that the anuria was due to concretions blocking the ureterovesical orifices, thus confirming the observations of Tsao and his co-workers⁸ and Carroll, Shea and Pike.⁹

That concretions may exist without blocking the ureters has been demonstrated by Plummer and

forced with close observation of the urinary output for the next forty-eight hours.

The conditions under which sulfapyridine hematuria and concretions develop are still not clear. Acidity of the urine has frequently been suggested as a factor and the simultaneous administration of sodium bicarbonate with the sulfapyridine to alkalize the urine has been advised. That this procedure is of little value has been demonstrated by clinical⁸ and experimental⁷ observations. In addition there has been observed in this hospital an instance of sulfapyridine hematuria developing in a patient receiving adequate amounts of sodium bicarbonate, whose urine was alkaline at the time of hematuria. Haviland and Bratton¹³ have shown that the solubility of acetyl sulfapyridine in urine remains essentially the same for a range of p_H 3.3-7.4, and that the solubility at p_H 7.9 is not enough to be of therapeutic advantage.

11. Plummer, Norman, and McLellan, Frederick: The Production of Sulfapyridine Renal Calculi in Man Following Administration of Sulfapyridine, J. A. M. A. 114: 943 (March 16) 1940.

12. Antopol and Robinson.⁸ Plummer and McLellan.¹¹

13. Personal communication to the authors from Dr. James W. Haviland and Dr. A. Calvin Bratton, Johns Hopkins University, Baltimore.

Another factor suggested and one which has seemed most likely, has been that of a low urinary output. The validity of this explanation, however, must be seriously challenged in the light of recent experience. In case 2 the urinary output would appear to have been quite adequate and, furthermore, instances have been observed in this clinic in which the urinary output has been far less without the development of hematuria or other associated symptoms. Moreover, Toomey, Reichle and Takacs⁷ have demonstrated that the administration of large quantities of fluid to the *Macaca mulatta* monkey has not prevented either the formation of stones or the development of pathologic changes in the urinary tract.

It is of interest that, in the cases presented in this report, acetylation of sulfapyridine both in the blood and in the urine was abnormally high. This has been true, in general, of the cases of sulfapyridine hematuria observed in this hospital,¹⁴ but it must be pointed out again that similar degrees of acetylation have been observed in cases which have not exhibited any sign of urinary abnormality.

Toomey and his co-workers⁷ have made the interesting observation that the sodium salt of sulfapyridine, when used in comparable doses, is more apt to produce toxic urinary symptoms than is sulfapyridine. The significance of this observation is not exactly clear at the present time.

In general, the pathologic changes in case 1 were entirely in accord with those found experimentally in monkeys by Antopol and Robinson.⁶ They consisted essentially of great tubular and capsular dilatation, marked congestion and vacuolization within the glomerular tufts, and an acute hemorrhagic pyelo-ureteritis extending into the adjacent renal medullary tissue. A similar pathologic description in man has been given by Tsao and his associates,⁸ and Plummer and McLellan¹¹ mention petechial hemorrhages in the pelvis of the kidney.

On the other hand, while Stryker¹⁵ found dilatation of the tubules and capsular spaces in the kidneys of a patient, he observed no changes in the mucosal surfaces of the urinary tract. He believes that certain basophilic masses found plugging the tubules are responsible for the tubular dilatation and represent crystals of precipitated drug. A few such masses were found in the collecting tubules of the kidneys described in the present case. Since the tissues were fixed in Zenker-acetic or in solution of formaldehyde and even washed during the staining process, it is possible that many more of these bodies were originally present. However, Strong¹⁶ has shown in recent animal experiments that some tubular and capsular dilatation can occur acutely from ureteral obstruction alone, so that this factor must be considered also in explaining the kidney changes in the case described in the present report.

SUMMARY

1. Two cases of complete anuria occurring during sulfapyridine therapy were observed.
2. In both cases anuria was due to calculi blocking the urinary tract at the ureterovesical orifices.
3. Treatment by means of cystoscopy was successful.

4. The pathologic changes in the upper urinary tract of a patient dying of a neurosurgical complication consisted essentially of great tubular and capsular dilatation, marked congestion and vacuolization within the glomerular tufts, and an acute hemorrhagic pyelo-ureteritis extending into the adjacent renal medullary tissue.

PERIPHERAL NEUROPATHY DUE TO VITAMIN B₁ DEFICIENCY IN DIABETES MELLITUS

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We are reporting nine cases of a symmetrical peripheral neuropathy due to vitamin B₁ deficiency found in a group of 422 ambulatory patients with diabetes mellitus. The occurrence of peripheral neuropathy in diabetic patients is well known and has been the subject of several reports since its description by Marchal de Calvi¹ in 1864. The incidence of this condition in groups of such patients varies, according to Jordan,² from 0.6 to 57.3 per cent. The extreme variation thus reported demands explanation and is due, in our opinion, to several factors. There is, first, a tendency on the part of many physicians to label vague pains in the extremities as neuritis without employing objective criteria for the diagnosis of peripheral neuropathy. Pain in the extremities of diabetic patients is common; it occurs in 17 per cent of Joslin's³ patients. Such pain, however, is more often due to arterial and venous circulatory disturbances, arthritis, myositis or mechanical and fatigue phenomena than to peripheral neuropathy resulting from vitamin B₁ deficiency. Another factor is the failure to perform an adequate neurologic examination, especially in the absence of a history of pain in the extremities. Pain, though nearly always present at some time during the course of peripheral neuropathy, may be absent by the time the patient is examined, and its history can be elicited only by leading questions.

That vitamin deficiency may be an etiologic factor in the peripheral neuropathy of diabetic patients was first pointed out by Wohl⁴ in 1926 on the basis of the dietary history, clinical observations and results of treatment with yeast and yeast concentrates of a patient with diabetes. Then in 1928 Angle⁵ noted improvement in a case of "diabetic tabes" following a diet rich in vitamins. The following year Minot⁶ encountered two diabetic patients with peripheral neuritis who improved slowly by taking large amounts of yeast concentrate. The work of Wechsler⁷ and of Root and Rogers⁸

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1. Marchal de Calvi, C. J.: Recherches sur les accidents diabétiques et essai d'une théorie générale du diabète, Paris, P. Asselin, 1864.

2. Jordan, W. J.: Neuritic Manifestations in Diabetes Mellitus, Arch. Int. Med. 57: 307 (Feb.) 1936.

3. Joslin, E. P.: The Treatment of Diabetes Mellitus, ed. 6, Philadelphia, Lea & Febiger, 1937.

4. Wohl, M. G.: Avitaminosis in the Course of Diabetes, J. A. M. A. 87: 901 (Sept. 18) 1926.

5. Angle, F. E.: Tabes Diabetica: Report of a Case, U. S. Nav. M. Bull. 26: 81 (Jan.) 1928.

6. Minot, G. R.: Some Fundamental Clinical Aspects of Deficiencies, Ann. Int. Med. 3: 216 (Sept.) 1929.

7. Wechsler, I. S.: Unrecognized Cases of Deficiency Polyneuritis (Avitaminosis?): Preliminary Report, M. J. & Rec. 131: 441 (May) 7) 1930.

8. Root, H. F., and Rogers, M. H.: Diabetic Neuritis with Paralysis, New England J. Med. 202: 1049 (May 29) 1930.

14. Blake, F. G., and Haviland, J. W.: Sulfapyridine in Pneumococcal, Streptococcal and Staphylococcal Infections, Tr. Am. Phys. 54: 130, 1939.

15. Stryker, W. A.: The Nature of the Renal Lesion with Sulfapyridine Therapy, J. A. M. A. 114: 953 (March 16) 1940.

16. Strong, K. C.: Plastic Studies in Abnormal Renal Architecture: V. The Parenchymal Alterations in Experimental Hydronephrosis, Arch. Path. 20: 77 (Jan.) 1940.

further suggested that these patients have, as a rule, an inadequate intake of food and vitamins and that their clinical and neuropathologic manifestations and response to treatment were similar to those of patients having beriberi.

Since then Vorhaus and his co-workers,⁹ in 1935 and Sciclounoff and Broccard¹⁰ in 1936, as a result of therapeutic application of thiamine hydrochloride, have stated that a deficiency of vitamin B₁ was the etiologic factor in the neuritis of diabetes. Unfortunately, neither of these groups described their criteria for the diagnosis of peripheral neuropathy or detailed the objective observations before and after treatment, although they mentioned in general pains, paresthesias, tenderness and altered reflexes.

On the other hand, Needles,¹¹ on the basis of careful dietary analysis, reported three cases of diabetes presenting definite peripheral neuropathy in which the diets were apparently adequate as judged by the vitamin

of peripheral neuropathy. A total of 422 patients were so examined. To avoid the diagnostic problem already discussed we have followed the criteria of one of us¹² for the diagnosis of peripheral neuropathy due to vitamin B₁ deficiency. These criteria require the presence of a definite bilateral symmetrical polyneuropathy involving first and predominantly the lower extremities. The minimum observations necessary to establish this diagnosis consist in sensory changes in a peripheral nerve distribution in the lower extremities (such as plantar hyperesthesia, which may extend up the ankles and legs in a sock distribution, tenderness of calf muscles and loss of position sense and of vibratory sensation, beginning first in the toes and later extending proximally) plus at least absence of ankle jerks. Peripheral neuropathy of this extent, limited to the lower extremities and with the knee jerks preserved, is designated as mild. If, in addition, the knee jerks are lost, the neuropathy is classified as moderate; if

TABLE 1.—Clinical Data

Case Number	Age	Sex	Duration Diabetes In Years	Diet			Insulin	Vitamin B ₁ Calory Ratio	Status of Diabetic Control	Complications
				Carbohydrate	Protein	Fat				
1	53	♀	2	130	65	85	None	4.3	Diabetes out of control and untreated until seen in clinic; therapy started at same time	Arteriosclerotic and hypertensive heart disease
2	67	♀	5	150	65	75	20-0-15	4.1	Diabetes well controlled	Toxic adenoma of thyroid
3	63	♂	2	300	65	85	None	3.28	Poorly nourished; lived in municipal lodging house; only small amounts of sugar in urine; diet eaten not the one prescribed	Arteriosclerotic and hypertensive heart disease; chronic diffuse glomerulonephritis
4	56	♂	½	150	65	65	None	4.1	Diabetes uncontrolled; sugar in urine; diabetes controlled after start of therapy	Mild general arteriosclerosis
5	64	♀	6	250	65	87	None	3.5	Diabetes controlled	Arteriosclerotic and hypertensive heart disease
6	56	♀	12	300	65	80	None	3.28	Patient did not follow diet; always moderate glycosuria	Essential hypertension; postoperative thyroid
7	50	♂	2	200	65	65	40-20-40	3.2	Moderate glycosuria	Essential hypertension
8	72	♂	30	150	65	85	10-0-10	4.1	Moderate glycosuria	General arteriosclerosis; chronic cholecystitis
9	59	♀	4	140	80	60	None	4.1	Occasional mild glycosuria	Essential hypertension; mild hyperthyroidism

B₁/calory ratio. A sample diet for a single day was utilized in these estimations. One of his patients freely admitted dietary infractions which would significantly lower this ratio. Substitution of food low in vitamin B₁ but containing equivalent carbohydrate and caloric values is frequent in all groups of diabetic patients and may explain how a prescribed adequate diet becomes actually inadequate in vitamin B₁.

The object of this study was to determine the incidence of definite peripheral neuropathy due to vitamin B₁ deficiency in a large group of diabetic patients and the response to specific therapy.

MATERIALS AND METHOD OF STUDY

The subjects in this study were all ambulant patients who attended the diabetic clinic of the Third (New York University) Division of Bellevue Hospital during 1939. Each patient was subjected to a neurologic examination specifically aimed at discovering evidence

there is involvement of the upper extremities, the spinal cord or the cranial nerves, or if a "central neuritis" is present, it is classified as severe. Peripheral neuropathy that involves a single nerve, that is not bilateral and symmetrical, or does not involve first and predominantly the lower extremities (in ambulatory patients) is excluded as probably not due to vitamin B₁ deficiency alone. For such neuritides other etiologic agents should be sought. These, such as lead, arsenic, triorthocresol phosphate and bacterial and virus infections, may and do operate in the diabetic as well as in the nondiabetic person, and the type of peripheral neuropathy they produce seldom fulfils the criteria for the diagnosis of neuropathy due to B₁ deficiency.

All patients in whom the objective criteria necessary for the diagnosis of mild peripheral neuropathy were found were designated as suitable for a therapeutic test. Those having only suggestive signs were excluded. The designated patients, without otherwise changing their diet, were given 10 mg. of synthetic thiamine hydrochloride by mouth daily throughout the period of observation; follow-up observations were performed

9. Vorhaus, M. G.; Williams, R. R., and Waterman, R. E.: Studies on Crystalline Vitamin B₁: Experimental and Clinical Observations, J. A. M. A. 105:1580 (Nov. 16) 1935.

10. Sciclounoff, François, and Broccard, Raymond: La vitamine B₁ dans le traitement des polyneuropathies, Schweiz. med. Wchnschr. 66:985 (Oct. 10) 1936.

11. Needles, William: Vitamin Studies in Cases of Diabetic Neuritis, Arch. Neurol. & Psychiat. 41:1222 (June) 1939.

12. Jolliffe, Norman: The Diagnosis, Treatment and Prevention of Vitamin B₁ Deficiency, Bull. New York Acad. Med. 15:469 (July) 1939.

weekly for a period of at least six months. All conditions remained constant except the adjustment of insulin as required.

RESULTS

Of a total of 422 patients, nine, or 2.1 per cent, fulfilled the criteria for the diagnosis of peripheral neuropathy resulting from vitamin B₁ deficiency. In these nine subjects there were no abnormal neurologic manifestations other than the peripheral neuropathy, and no other clinically evident vitamin deficiencies. In table 1 are presented the clinical data, such as age, sex, duration of diabetes, diet, use of insulin, status of diabetic control and complications. None of these patients had evidence of ketosis during the period of study. There were four men and five women, the ratio of males to females in the entire group of 422 subjects being approximately the same. All nine subjects were 50 years of age or over, while 69 per cent of the whole group of 422 patients were over 49 years of age. The known duration of the diabetes of the nine patients varied from six months to thirty years, with an average of 6.7 years. The average duration of diabetes in the 422 patients was 8.3 years.

The neurologic observations and the results of therapy are summarized in table 2. Tenderness of the calf muscles, plantar hyperesthesia and loss of ankle jerks were present in all nine subjects; some degree of loss of vibratory sensation was found in three, while the position sense was intact in all. No subject showed more than mild peripheral neuropathy according to our criteria. After therapy, plantar hyperesthesia disappeared in all cases after four weeks and in three after two weeks. Tenderness of the calves disappeared in all cases after six weeks and in five cases after two weeks. Vibratory sensation in the toes was absent in three subjects, returning to normal after eight and ten weeks respectively in two subjects but remaining absent in the toes of one subject (case 3) after six months of treatment. The ankle jerks returned after two weeks in one subject and within fourteen weeks in eight subjects; in one subject (case 3) they had not returned at the end of six months.

Some patients not tabulated in this study complained of persistent unilateral pain in an extremity, while others experienced vague aches and pain in the extremities. Neurologic examination of these patients disclosed no objective signs of bilateral symmetrical peripheral neuropathy. These subjects were treated with thiamine hydrochloride, vegex or brewers' yeast. The results were not uniform. In some the relief was apparently sustained; in others it was temporary, while in still others no relief was experienced.

COMMENT

We believe that the symmetrical peripheral neuropathy found in these nine diabetic patients was due to vitamin B₁ deficiency. This belief is based on the following reasons: First, the clinical characteristics fulfilled the established criteria for the diagnosis of peripheral neuropathy due to vitamin B₁ deficiency; second, without otherwise changing the diet or therapy, the addition of 10 mg. of synthetic thiamine hydrochloride daily by mouth was followed by cure in eight cases and by objective improvement in the ninth.

The explanation of the development of peripheral neuropathy due to vitamin B₁ deficiency in these nine subjects is speculative, but in our opinion it is due

directly to eating a diet of borderline adequacy in vitamin B₁. On the basis of Cowgill's¹³ prediction formula, the diets prescribed for these patients were all adequate in that the vitamin B₁/calory ratio ranged from 3.2 to 4.3, representing an excess of 140 to 210 per cent over their predicted minimal requirements. One of us¹⁴ has recently suggested that diets representing a vitamin B₁/calory ratio of 2.3 or more are definitely adequate, those less than 1.7 are definitely inadequate, and those between 1.7 and 2.3 are of borderline adequacy. By this criterion all the prescribed diets were above the borderline range, furnishing safety margins of from 39 to 87 per cent. As we had previously pointed out, however, substitution of foods poor in vitamin B₁ (such as white bread or crackers) but con-

TABLE 2.—Number of Weeks After Beginning of Treatment When Reversal of Symptoms Were Noted*

Case	Weeks of Treatment	Sensory			Motor	
		Calf Tenderness	Plantar Hyperesthesia	Vibratory Sensation in Toes	Ankle Jerks	Knee Jerks
1	0	+	+	N	0	+
	3	0	0	N	0	+
	8	0	0	N	+	+
2	0	+	+	N	0	+
	3	0	+	N	0	+
	4	0	0	N	0	+
3	0	0	0	N	+	+
	0	+	+	0	0	+
	2	0	+	0	0	+
4	0	+	+	0	0	+
	4	+	0	0	0	+
	6	0	0	0	0	+
5	0	+	+	N	+	+
	3	0	0	N	+	+
	4	0	0	N	+	+
6	0	+	+	N	0	+
	2	0	0	N	0	+
	4	0	0	N	+	+
7	0	+	+	N	0	+
	2	0	+	N	0	+
	3	0	0	N	0	+
8	12	0	0	0	+	+
	0	+	+	0	0	+
	2	0	0	0	0	+
9	8	0	0	+	0	+
	14	0	0	+	+	+
	0	+	+	N	0	+
	2	0	0	N	+	+

* 0 indicates absence; +, presence, and N normal.

taining equivalent carbohydrate and caloric values for prescribed foods richer in vitamin B₁ is common in all groups of diabetic patients. This was especially true in our patients because of their poor economic condition. In view of this it is surprising that a peripheral symmetrical polyneuropathy developed in but 2.1 per cent of the patients. There are, moreover, several other possible contributory factors. The most important of these, we believe, may be arteriosclerosis. This is suggested by the age distribution of our patients. Woltman and Wilder,¹⁵ in a study of the peripheral nerves of ten diabetic patients, observed arteriosclerosis of the small arteries in the nerve tunnels of the legs of all subjects and areas of degeneration in the nerves of nine subjects. This vascular inadequacy may require a

13. Cowgill, G. R.: The Vitamin B Requirement of Man, New Haven, Conn., Yale University Press, 1934.

14. Jolliffe, Norman: A Clinical Evaluation of the Adequacy of Vitamin B₁ in the American Diet, Internat. Clin. 4: 46 (Dec.) 1938.

15. Woltman, H. W., and Wilder, R. M.: Diabetes Mellitus: Pathologic Changes in the Spinal Cord and Peripheral Nerves, Arch. Int. Med. 41: 576 (Oct.) 1929.

higher concentration of thiamine in the blood, to provide sufficient vitamin to the nerves, than in subjects with normal arteries, as pointed out by Naide.¹⁶ Another factor may be the polyuria¹⁷ accompanying glycosuria, which, if persistent, may cause an increased excretion of vitamin B₁ in the urine, rendering it less available for use by the body. This factor may have played a role in six of our nine subjects who, because of lack of cooperation, either voluntary or due to economic circumstances, showed persistent though moderate glycosuria without ketosis. Another factor, of doubtful importance, may be the presence of a disturbance in carbohydrate metabolism in diabetic persons which might conceivably interfere with the utilization of thiamine hydrochloride. Too little is known concerning this relationship to deny its influence, but two facts are available that cast doubt on its significance. The first is that peripheral neuropathy in our subjects occurred in the older age group with relatively mild diabetes, rather than in the younger group with the more severe diabetes. The second fact is that thiamine hydrochloride administered by mouth caused prompt improvement, showing that these diabetic patients could utilize from this amount of the vitamin given by mouth enough to cure or improve the clinical manifestations of the deficiency. Another factor, which does not seem to apply to any of our patients but which under certain conditions may be contributory, is the institution of insulin therapy and the resulting increased utilization of carbohydrate. In subjects whose stores and intakes of vitamin B₁ are of borderline adequacy, the increased utilization of carbohydrate will require additional vitamin B₁. Unless precautions are instituted, polyneuropathy may result from vitamin B₁ deficiency. Hausman¹⁷ has recently observed three such cases. In this connection it is interesting to note that Sydenstricker, Geeslin and Weaver¹⁸ observed the development of clinical signs of pellagra in two diabetic patients when the carbohydrate content of the diet was increased and added insulin was administered to insure utilization of the augmented diet. They concluded that, "under chronic conditions, signs of avitaminosis might be expected to appear, with or without ketosis, when unusually rapid dextrose metabolism is brought about by the use of insulin."

SUMMARY

We have studied 422 ambulant diabetic patients. Nine (2.1 per cent) had a symmetrical peripheral neuropathy characteristic of the peripheral neuropathy found in subjects having proved vitamin B₁ deficiency. Treatment by daily administration of 10 mg. of thiamine hydrochloride by mouth, without otherwise changing the regimen, resulted in cure of eight subjects and improvements in the ninth.

Indifferent or inconsistent results were obtained on treating neuropathy of single nerves or the vague aches and pains of the diabetic patient.

CONCLUSIONS

The symmetrical peripheral neuropathy beginning first in, and involving primarily, the lower extremities of patients having diabetes mellitus responds to thiamine hydrochloride and in our opinion is due to vitamin B₁ deficiency.

THE COEXISTENCE OF BRUCELLA INFECTION AND HODGKIN'S DISEASE

A CLINICAL, BACTERIOLOGIC AND IMMUNOLOGIC STUDY

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The isolation of *Brucella melitensis* from cultures of lymph nodes from patients having Hodgkin's disease opened an interesting field of investigation.¹ Subsequently fourteen consecutive cases of Hodgkin's disease have been studied carefully for evidence of *Brucella* infection. The clinical, bacteriologic and immunologic observations in seven cases in this series are presented in detail and in the remainder are summarized briefly.

Cultures have been taken of a part of every excised lymph node² and the remaining part has been prepared for pathologic study. In every case the clinical diagnosis of Hodgkin's disease has been confirmed by histologic section of the lymph nodes, taken for biopsy, and the existence of *Brucella* infection has been demonstrated by the isolation of the organisms from either the blood or the lymph nodes or both. The agglutinin-absorption tests and the bacteriostatic reactions of dyes have been used to determine the species of *Brucella*. The technics used for the agglutination reaction and for the determination of the opsonocytaphagic index have been previously reported.³ Because the *Brucella* organisms isolated from patients with Hodgkin's disease have been found to differ significantly from the usual laboratory strains,⁴ agglutination reactions and opsonocytaphagic index determinations have recently been carried out both with the usual laboratory *Brucella* strain and with an encapsulated strain isolated from a patient having Hodgkin's disease. The opsonocytaphagic index number has been calculated by the method of Foshay and Le Blanc.⁵

The cases are reported here in the sequence in which they came under observation.

REPORT OF CASES

CASE I.—R. P., a white man aged 24, who entered the hospital on Oct. 26, 1938, had become ill in November 1937 with enlargement of the right cervical lymph nodes and he was treated by excision and superficial radium therapy. At the time of entry a lymph node from 3 to 4 cm. in diameter and several smaller nodes were palpable in the right cervical region. *Brucella melitensis* var. *suis* was isolated from a right cervical lymph node which had the characteristic histopathologic appearance of Hodgkin's disease. The enlarged lymph nodes regressed under treatment with sulfanilamide and serum from a person considered immune to *Brucella* infection. The patient was discharged from the hospital Dec. 27, 1937, and was followed at close intervals. There was no evidence of activity

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1. Parsons, P. B., and Poston, Mary A.: The Pathology of Human Brucellosis, South. M. J. 32: 7-13 (Jan.) 1939. Poston and Parsons.¹

2. Poston, Mary A., and Parsons, P. B.: Isolation of *Brucella* from Lymph Nodes, J. Infect. Dis. 66: 86-90 (Jan.-Feb.) 1940.

3. Menefee, E. E., Jr., and Poston, Mary A.: Significance of Standard Laboratory Procedures in the Diagnosis of Brucellosis, Am. J. M. Sc. 197: 646-653 (May) 1939.

4. Mickle, W. A.: Capsule Formation by Members of the *Brucella* Group, J. Infect. Dis. 66: 271 (May-June) 1940.

5. Foshay, Lee, and Le Blanc, T. J.: The Derivation of an Index Number for Opsonocytaphagic Test, J. Lab. & Clin. Med. 22: 1297-1309 (Sept.) 1937.

16. Naide, Meyer: The Use of Vitamin B₁ in Rest Pain of Ischemic Origin, Am. J. M. Sc. 197: 766 (June) 1939.

17. Hausman, Louis: Personal communication to the authors.

18. Sydenstricker, V. P.; Geeslin, L. E., and Weaver, J. W.: Avitaminosis Occurring in Diabetic Patients Under Insulin Therapy, J. A. M. A. 113: 2137 (Dec.) 1939.

of the Hodgkin's disease process until January 1940, when the right cervical lymph nodes again enlarged. Repeated cultures taken of the blood and lymph nodes have been negative.

It is considered that further observation is necessary to determine the true significance of the isolation of *Brucella* from this patient.

CASE 2.—*Enlargement of cervical, axillary, inguinal and mediastinal lymph nodes of ten months' duration; culture of a cervical node yielded Brucella melitensis var. melitensis; regression of enlargement of lymph nodes under sulfapyridine therapy; recurrent enlargement of inguinal and femoral lymph nodes on the left; Brucella melitensis var. melitensis isolated from blood cultures; treatment with sulfapyridine and immune serum; temporary improvement.*

M. W., a Negro boy aged 5 years, who was brought to the hospital Nov. 16, 1938, had enlargement of the neck of ten months' duration. In February 1938 a firm, painless swelling appeared below the angle of the left jaw which alternately subsided and recurred. For a week preceding the hospital visit the patient had had a mild cold with nonproductive cough, and a tender swelling had appeared in the left groin.

On physical examination the temperature was 37 C. (98.6 F.), the pulse rate 120 and the respiratory rate 20. The child was well nourished and did not appear ill. There was a firm, nontender mass of lymph nodes measuring 6 by 8 cm. in the left cervical region. The right cervical nodes were enlarged to a lesser degree. The left axillary nodes were markedly enlarged, one node measuring 4 cm. in diameter. The right axillary and inguinal nodes were enlarged. Retromanubrial dullness measured 5 cm. The heart and lungs were not remarkable. There was no abdominal tenderness and no organs were palpable. On rectal examination a firm, nontender mass was felt on the left side.

Wassermann and Kahn reactions of the blood were negative; examination of the blood showed hemoglobin 62 per cent, white blood cells 16,700, with polymorphonuclear leukocytes 80 per cent (stab cells 12 per cent), eosinophils 0, basophils 0, large lymphocytes 3 per cent, small lymphocytes 17 per cent and monocytes 0; *Brucella* agglutination was negative; an intracutaneous tuberculin test (1:1,000) gave negative results.

Permission for the biopsy of a lymph node was refused and the patient was not seen again until December 7. His condition had remained unchanged until the preceding five days, when loss of appetite and an evening elevation of temperature developed. Physical examination was unchanged except for a slight increase in the size of the enlarged lymph nodes. Biopsy of a cervical node confirmed the clinical diagnosis of Hodgkin's disease and a culture taken of this node yielded *Brucella melitensis var. melitensis*. Admission to the hospital was advised but the patient did not return until Jan. 26, 1939.

The physical condition at this admission was unchanged except for further slight enlargement of the lymph nodes. The temperature was 39.5 C. (103.1 F.), pulse rate 140 and respiratory rate 24. A blood count revealed hemoglobin 62 per cent, red blood cells 3,140,000 and white blood cells 20,000, polymorphonuclear leukocytes 82 per cent (stab cells 53 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 4 per cent, small lymphocytes 9 per cent, monocytes 4 per cent. Roentgenograms of the chest showed a large mass in the superior mediastinum. Bacteriologic and immunologic studies are given in chart 1.

At bed rest the patient's temperature fell to 37.5 C. (99.3 F.) on the third hospital day, at which time administration of sulfapyridine was started but it was discontinued after one week because of leukopenia. Throughout the administration of sulfapyridine the patient was afebrile, but four days after discontinuation of the drug his temperature rose to 39.5 C. (103.1 F.) and remained elevated for two days. Blood cultures were sterile. Under sulfapyridine therapy there was a progressive and marked decrease in the size of the superficial lymph nodes, and x-ray examination showed marked diminution in the size of the mediastinal mass. A lymph node excised on February 11 again showed the histopathologic picture of Hodg-

kin's disease. A culture taken of this node yielded diphtheroids. The patient had improved greatly by the time of discharge on March 3 and appeared well when visited at home on March 18.

The patient was readmitted to the hospital on May 17, having felt well in the interval. The temperature was 36.8 C. (98.6 F.). There was no recurrent enlargement of the cervical, axillary and right inguinal lymph nodes but there was definite enlargement of the left inguinal and femoral nodes. Hemoglobin was 59 per cent; red blood cells numbered 3,020,000, white blood cells 8,800, polymorphonuclears 52 per cent, eosinophils 2 per cent, basophils 0, large lymphocytes 6 per cent, small lymphocytes 34 per cent and monocytes 6 per cent. Cultures taken of an inguinal node on the left side which gave the pathologic appearance of Hodgkin's disease were sterile. A roentgenogram of the chest showed complete absence of the mass originally noted in the superior mediastinum.

On May 19 sulfapyridine was given but was discontinued on May 27 because of severe nausea and vomiting. On May 22 the patient's temperature, previously not above 37.8 C. (100 F.), rose to 39 C. (102 F.) and remained elevated for four days. At this time *Brucella melitensis var. melitensis* was isolated from the blood. Ten cc. of bovine antimelitensis serum was given intramuscularly on May 24 and 25, with a subsequent prompt fall of temperature to normal. The left inguinal and

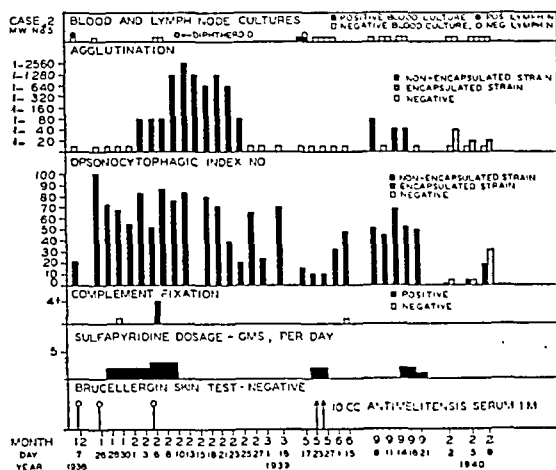


Chart 1.—Bacteriologic and immunologic studies in case 2.

femoral lymph nodes gradually decreased in size. On May 29 the patient complained of generalized itching of the skin and a mild exfoliative dermatitis developed. He was discharged from the hospital greatly improved on June 4.

The patient was readmitted to the hospital on September 8. He had been well until one week previously, when an evening fever developed and recurrent enlargement of the left cervical, axillary and inguinal lymph nodes. The temperature was 37.4 C. (99.3 F.). The patient did not appear ill. The firm, nontender cervical nodes were barely palpable. In the left axilla was a mass of firm, nontender nodes measuring 5 by 6 cm. The inguinal nodes were similarly enlarged. A large, firm, nontender mass measuring 6 by 6 cm. was felt over the right external iliac vessels. On rectal examination a similar smaller mass was felt on the left side.

Examination of the blood revealed hemoglobin 58 per cent, red blood cells 2,750,000, white blood cells 5,200, polymorphonuclears 44 per cent (stab cells 3 per cent), eosinophils 2 per cent, basophils 0, large lymphocytes 3 per cent, small lymphocytes 36 per cent, monocytes 15 per cent. The corrected sedimentation rate was 28 mm. per hour. A roentgenogram of the chest showed no mediastinal or hilar enlargement.

An elevation of temperature to 38.6 C. (101.5 F.) was noted on the second hospital day. Thereafter the patient was afebrile for one week, when the temperature rose to 38.2 C. (100.7 F.). At this time sulfapyridine was given for one week, during which time the fever promptly ceased and there was marked

regression of lymph node enlargement by the time of discharge on September 23.

The patient returned to the hospital on Feb. 2, 1940. In the interval he had had occasional episodes of fever and malaise lasting several days. One week before his return there was transient enlargement of the left cervical lymph nodes.

The temperature was 37.4 C. (99.3 F.). The left cervical lymph nodes were firm and nontender and measured from 2 to 3 cm. in diameter. The right cervical, axillary and inguinal nodes were smaller, firm and nontender. On rectal examination a few small, firm nodes were palpable on the left.

Examination of the blood revealed hemoglobin 68 per cent, red blood cells 3,760,000, white blood cells 12,600, polymorphonuclears 69 per cent (stab cells 1 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 2 per cent, small lymphocytes 27 per cent, monocytes 1 per cent; corrected sedimentation rate 28 mm. per hour. A roentgenogram of the chest was not remarkable.

During the patient's hospital stay there was an occasional elevation of temperature to 37.7 C. (99.8 F.). No treatment was given and the patient's condition was unchanged at discharge on February 11.

The initial marked regression of the widespread enlargement of lymph nodes under sulfapyridine therapy in this case was striking. It is noteworthy that the

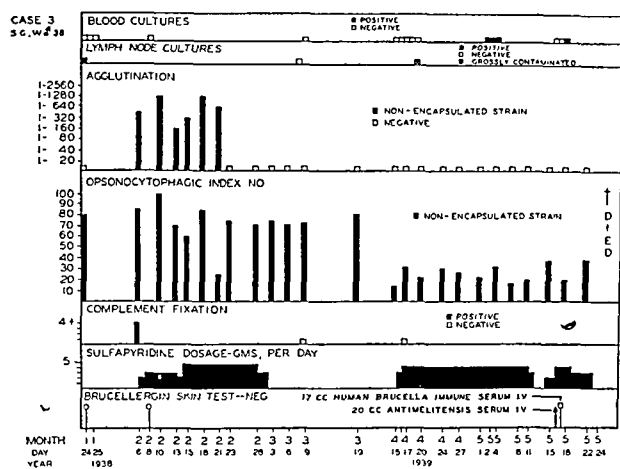


Chart 2.—Bacteriologic and immunologic studies in case 3.

appearance of serum agglutinins and marked phagocytosis coincided with this clinical improvement. Subsequently *Brucella melitensis* var. *melitensis* was isolated from blood cultures, taken during a febrile episode and shortly after recurrent enlargement of the left inguinal and femoral lymph nodes. After administration of antimelittensis serum and sulfapyridine there was prompt subsidence of fever and lymph node enlargement. No evidence of an immune response existed at the time *Brucella melitensis* var. *melitensis* was isolated from the blood, nor has there been any significant immune response during subsequent periods of activity of the disease process. The clinical course, which has appeared to be influenced by treatment directed toward control of the *Brucella* infection, can be correlated closely enough with the cultural and immunologic observations to suggest that a great part of the clinical picture presented by this patient with Hodgkin's disease might be explained by the coexisting *Brucella* infection.

CASE 3.—Left supraclavicular lymph node enlargement; roentgen therapy; fever and enlargement of liver and spleen, isolation of *Brucella melitensis* var. *melitensis* from lymph node and blood cultures; treatment with sulfapyridine; death one year after onset.

S. G., a white man aged 38, admitted to the hospital Jan. 20, 1939, complained of abdominal pain of five weeks' duration.

His illness began in April 1938 with a gradual onset of weakness, painless progressive enlargement of the left supraclavicular lymph nodes and intermittent sharp pain in the lower part of the abdomen radiating to both lumbar regions. A loss of weight of from 20 to 30 pounds (9 to 13.6 Kg.) occurred during the first month of illness. Roentgen therapy was given to the left supraclavicular region during April and May 1939, with prompt regression of lymph node enlargement and improvement in the patient's general condition. The patient was relatively well and able to work until December 1938, when so-called flu developed, with malaise, fever and night sweats. At this time severe "knifelike" para-umbilical pain, radiating to both lumbar regions, appeared and persisted.

The temperature was 38.5 C. (101.3 F.), pulse rate 104, respiratory rate 22 and blood pressure 110 systolic, 72 diastolic. The patient was malnourished and appeared chronically ill. Small, firm, nontender cervical and axillary nodes were palpable on the left side. There was no other enlargement of the lymph nodes. The abdomen was distended and tympanitic but not tender. The liver edge was percussed 3 cm. below the costal margin. The spleen was palpable at the costal margin.

Wassermann and Kahn reactions of the blood were negative; hemoglobin was 61 per cent; red blood cells numbered 3,570,000, white blood cells 5,900, polymorphonuclears 85 per cent (stab cells 2 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 4 per cent, small lymphocytes 3 per cent and monocytes 7 per cent. The corrected sedimentation rate was 24 mm. per hour; roentgenographic examinations of the chest and gastrointestinal tract were negative except for an inconstant defect of the duodenal cap thought to be due to extrinsic pressure. Histologic section of an axillary lymph node showed lymphadenitis suggestive of Hodgkin's disease and cultures taken of this node yielded *Brucella melitensis* var. *melitensis*. Bacteriologic and immunologic studies are given in chart 2.

At rest in bed the patient's temperature varied between 38 and 39 C. (100.4 and 102 F.). Administration of sulfapyridine was started on February 7 but was discontinued on March 1 because of leukopenia and anemia. During sulfapyridine therapy the patient became afebrile, the abdominal pain disappeared and the liver and spleen decreased in size. Cultures taken of a lymph node excised on March 8 were sterile. This node again showed a histopathologic picture suggestive of Hodgkin's disease. The patient was much improved at the time of discharge, March 11, although for the three preceding days an elevation of temperature to 38.4 C. (101.1 F.) was noted.

The patient remained well for one week and then an infection of the upper respiratory tract developed, following which he became acutely ill and was readmitted to the hospital April 15.

The temperature was 38.9 C. (102 F.), pulse rate 124, respiratory rate 24, and blood pressure 110 systolic, 80 diastolic. The patient was markedly emaciated and acutely ill. The essential physical conditions were unchanged.

Hemoglobin was 60 per cent, red blood cells numbered 3,000,000, white blood cells 12,320, polymorphonuclears 92 per cent (stab cells 7 per cent, juveniles 1 per cent), eosinophils 0, basophils 0, large lymphocytes 3 per cent, small lymphocytes 3 per cent, monocytes 2 per cent. The corrected sedimentation rate was 26 mm. per hour. A roentgenogram of the chest showed no significant change. An examination of the gastrointestinal tract again showed inconstant deformity of the duodenal bulb. *Brucella melitensis* var. *melitensis* was isolated from blood cultures. Sections of an axillary lymph node showed the microscopic appearance of Hodgkin's disease. Cultures taken of this node were grossly contaminated.

The patient's course was characterized by fever and progressive cachexia, terminating in death six weeks after admission. Sulfapyridine was started on the second hospital day and was continued until the day before death. Repeated blood transfusions were given. On May 14, intravenous administration of bovine antimelittensis serum had to be stopped after 20 cc. had been given because of severe pain in the back. Seventeen cc. of blood serum from a person who had recovered from *Brucella* infection was given intravenously on May 20. Signs of focal pneumonia appeared and the patient sank into coma and died May 24.

Necropsy showed Hodgkin's disease involving the spleen, liver, kidneys and all lymph nodes, especially the retroperitoneal

and abdominal nodes. Cultures taken of the liver, a splenic lesion, lungs, pancreas, testicle, bile and of many lymph nodes yielded *Brucella melitensis* var. *melitensis*.

When this patient first came under observation, Hodgkin's disease with extensive abdominal involvement was considered to be the probable diagnosis. It should be emphasized, however, that the diagnosis of Hodgkin's disease was not established until six weeks before death. The histopathologic appearance of the first lymph nodes of which a biopsy was made was suggestive, but conclusive evidence of Hodgkin's disease was not obtained until a third biopsy was made. On the contrary, the presence of *Brucella* infection was demonstrated by isolation of the organism from the first lymph node biopsy five months before death and from subsequent blood cultures. Coincident with this clinical improvement was the appearance of serum agglutinins and marked phagocytosis. However, evidence of immunity to *Brucella* subsequently disappeared during the rapidly progressive phase of the disease, which was characterized by fever, cachexia and bacteremia. At necropsy Hodgkin's disease was widespread, and cultures taken of numerous lymph nodes and of the liver, spleen, pancreas, testicle and bile yielded *Brucella melitensis* var. *melitensis*.

CASE 4.—W. D., a white man aged 31, who entered the hospital Feb. 14, 1939, complained of intermittent fever, malaise and loss of weight of two years' duration. Coincident with the onset of these symptoms a tender swelling was noted in the right cervical region which regressed after roentgen therapy, but the systemic symptoms continued. Several weeks before entry enlargement of the right cervical lymph nodes was noted. Several firm, nontender right cervical nodes, about 2 cm. in diameter, were felt, and there was slight enlargement of the left cervical and axillary nodes. The spleen was palpable at the costal margin. Biopsy of a cervical lymph node established the diagnosis of Hodgkin's disease. Cultures of the nodes were sterile. Under treatment with sulfapyridine there was a definite decrease in the size of the enlarged lymph nodes. This treatment had to be discontinued because of the development of icterus, which persisted. The patient's subsequent course was characterized by Pel-Ebstein fever and progressive cachexia. Death occurred November 22. Permission for necropsy was not obtained. *Brucella melitensis* var. *suis* was isolated from the blood during the last four months of life.

CASE 5.—Generalized pruritus of nine months' duration; right cervical and mediastinal lymph node enlargement; isolation of *Brucella melitensis* var. *suis* from blood and lymph node cultures; treatment with sulfapyridine; no improvement.

P. T., a white woman aged 31, who entered the hospital on Feb. 18, 1939, complained of generalized pruritus of nine months' duration. No cutaneous lesions other than scratch marks had been noted. Three weeks before admission she noticed prominence of a vein in the left side of her neck. A loss of 10 pounds (4.5 Kg.) had occurred.

On physical examination the temperature was 36.9 C. (98.4 F.), pulse rate 110, blood pressure 124 systolic, 82 diastolic. The patient was malnourished but did not appear ill. The skin was rough and dry; no lesions were noted. In the right cervical region a firm, nontender mass of lymph nodes, each about 1 cm. in diameter, was felt. Elsewhere there was no enlargement of the lymph nodes. The left external jugular vein was greatly distended. The chest and abdomen were not remarkable.

Wassermann and Kahn reactions of the blood were negative; hemoglobin was 77 per cent; red blood cells numbered 3,880,000 and the white blood cells 10,150, polymorphonuclears 67 per cent, eosinophils 8 per cent, basophils 0, large lymphocytes 5 per cent, small lymphocytes 8 per cent, monocytes 12 per cent; a roentgenogram of the chest showed a large mass in the superior mediastinum. A specimen taken from a right cervical lymph node for biopsy confirmed the diagnosis of Hodgkin's

disease. *Brucella melitensis* var. *suis* was isolated from this node and from the blood. Immunologic studies are given in chart 3.

The patient was afebrile throughout her hospital stay. Sulfapyridine was given daily in doses up to 4 Gm. She was discharged March 10 but was closely followed and continued to take sulfapyridine. By March 27 there had been a definite reduction in the size of the right cervical nodes and pruritus had lessened. X-ray examination showed no change in the size of the mediastinal mass. Sulfapyridine was discontinued on April 3.

The patient returned on April 19 complaining of intensified pruritus of four days' duration. Physical examination was unchanged except for enlargement of a single, firm, nontender lymph node just above the right clavicle. A roentgenogram showed no change in the size of the mediastinal mass. Admission to the hospital for further treatment was advised but the patient refused. Sulfapyridine was taken irregularly from April 22 to April 30. The patient's condition was unchanged when last seen, May 1, 1939.

In this case there was definite reduction in the size of the enlarged right cervical lymph nodes under sulfapyridine therapy and pruritus improved, although no actual decrease in the size of the mediastinal mass could

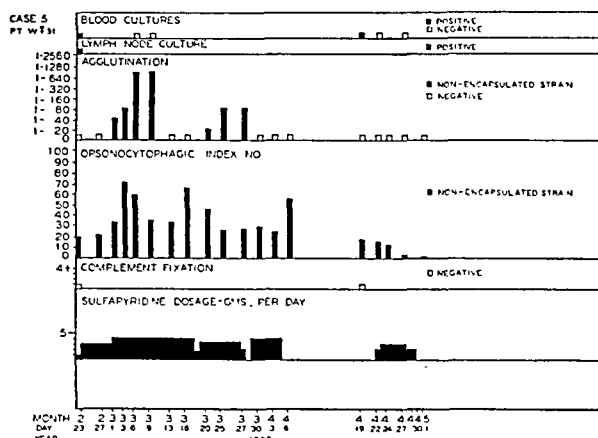


Chart 3.—Bacteriologic and immunologic studies in case 5.

be demonstrated roentgenologically. Serum agglutinins and significant degrees of phagocytosis appeared during the course of therapy but were not well sustained and were completely lacking with the recurrence of superficial lymph node enlargement, intensified pruritus and bacteremia. At this time *Brucella melitensis* var. *suis* was isolated from the heart's blood of two guinea pigs, which died nine days after intraperitoneal injection of 2 cc. of the patient's citrated blood.⁶

CASE 6.—C. I., a white woman aged 49, complained that in June 1938 fatigability and intermittent fever developed, with gradual painless enlargement of the superficial lymph nodes. Examination in January 1939 revealed marked enlargement of cervical, axillary, mediastinal and inguinal lymph nodes, and the liver and spleen were palpable. Biopsy of a lymph node established the diagnosis of Hodgkin's disease. Under roentgen therapy enlargement of the lymph nodes disappeared, the spleen and liver were no longer palpable and the fever subsided. She entered the hospital two weeks after completion of the roentgen therapy. Several firm, nontender cervical nodes on the right, from 2 to 3 cm. in diameter, were palpable. An excised lymph node showed marked fibrosis attributed to roentgen therapy and a culture taken of this node yielded *Streptococcus viridans*. The patient was closely followed and on May 1 slight enlargement of a right cervical node and an elevation of temperature

6. Poston, Mary A.: Studies on Chronic Brucellosis: III. Methods Used in Obtaining Cultures, Pub. Health Rep. 53:1-4 (Jan. 7) 1938.

were noted. *Brucella melitensis* var. *melitensis* was isolated from a blood culture taken on May 27, 1939. The patient was readmitted to the hospital June 6. There were daily elevations of temperature to 37.9 C. (100.2 F.), the spleen was palpable but there was no further enlargement of the lymph nodes. Under treatment with sulfapyridine and bovine anti-melitensis serum the fever subsided, the cervical lymph nodes decreased in size and the spleen was no longer palpable at the time of discharge, June 15. Repeated blood cultures were sterile. Since this time there has been no evidence of activity of the Hodgkin's disease process.

CASE 7.—Generalized pruritus with intermittent left cervical and axillary lymph node enlargement of three years' duration; initial treatment with sulfapyridine; recurrence of lymph node enlargement with stomatitis; cultures taken of oral lesions and of blood yielded *Brucella melitensis* var. *melitensis*; treatment with sulfapyridine and immunotransfusion; subsequent recurrence of cervical and axillary lymph node enlargement, appearance of mediastinal enlargement and fever; temporary improvement under roentgen therapy.

M. T., a white woman aged 31, first visited the hospital Nov. 4, 1937, complaining of generalized itching of one year's duration. Her illness began in the autumn of 1936 with persistent generalized itching and no cutaneous lesions other than excoriations caused by scratching. There had been progressive

22 and blood pressure 142 systolic, 80 diastolic. The patient was malnourished but did not appear ill. She constantly scratched all parts of her body, over which the skin was thickened, dry, a light brown and covered with numerous excoriations. The firm, nontender cervical lymph nodes, particularly those on the left, were enlarged to from 2 to 3 cm. in diameter. The left axillary nodes were enlarged to a slightly less degree. Elsewhere the superficial lymph nodes were barely palpable. The heart and lungs were not remarkable. There was no abdominal tenderness and no organs or masses were felt.

The Wassermann and Kahn reactions were negative; a blood count revealed hemoglobin 78 per cent, red blood cells 4,200,000, white blood cells 14,040, polymorphonuclears 76 per cent, eosinophils 11 per cent, basophils 1 per cent, large lymphocytes 4 per cent, small lymphocytes 6 per cent, monocytes 2 per cent. A roentgenogram of the chest was negative. Biopsy of a cervical lymph node confirmed the diagnosis of Hodgkin's disease. Cultures of the node were sterile. Bacteriologic and immunologic studies are given in chart 4.

Sulfapyridine was started on March 9 and was continued throughout her hospital stay. An occasional elevation of temperature to 38.5 C. (101.3 F.) was noted. The enlarged lymph nodes had decreased markedly in size and pruritus was much improved by the time of discharge, April 4.

For two weeks preceding her return on April 24 the patient noted a gradual recurrence of all her symptoms. The tempera-

ture was 37.2 C. (98.9 F.), pulse rate 90 and respiratory rate 20. The only change in her physical manifestations related to the size of the lymph nodes. The firm, discrete and nontender left cervical and axillary nodes were again enlarged, being from 2 to 3 cm. in diameter. The right cervical and axillary nodes were enlarged to a lesser degree. Hemoglobin was 81 per cent, red blood cells numbered 4,080,000 and white blood cells, 14,400, polymorphonuclears 74 per cent (stab cells 9 per cent), eosinophils 2 per cent, basophils 0, large lymphocytes 2 per cent, small lymphocytes 17 per cent and monocytes 5 per cent. A roentgenogram showed two small areas of density in the right

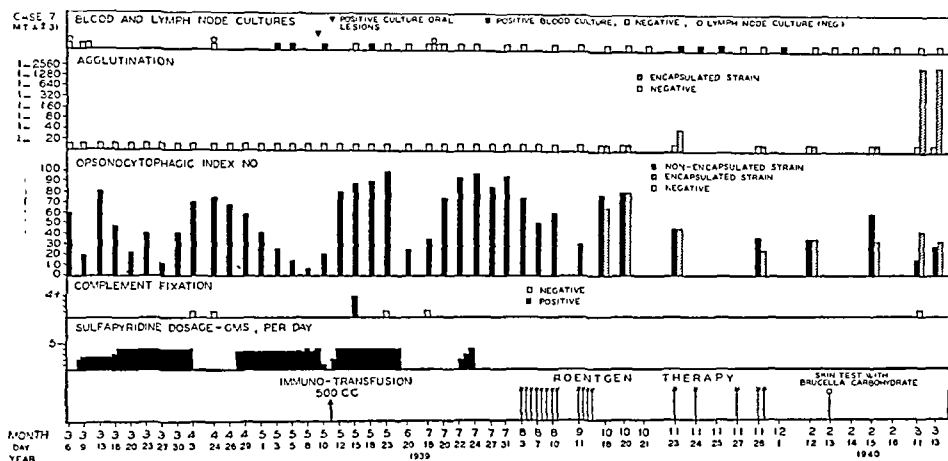


Chart 4.—Bacteriologic and immunologic studies in case 7.

abdominal enlargement and amenorrhea for the past five months, the patient considering herself pregnant.

The temperature was 37.7 C. (99.8 F.), the pulse rate 80, respiratory rate 20 and blood pressure 110 systolic, 65 diastolic. The patient was well nourished and did not appear ill. Small excoriations were scattered over the dry and scaly skin. No lymph nodes were palpable. Heart and lungs were not remarkable. The abdomen was symmetrically enlarged; the uterine fundus extended 22 cm. above the umbilicus. The clinical impression was neurogenic pruritus accentuated by pregnancy.

The patient returned on March 6, 1939, thirteen months after delivery of a normal fetus at term; she still complained of itching, which had continued with only brief periods of abatement. Enlargement of several left cervical and axillary lymph nodes had been noted for two months. On close questioning it was found that at the onset of her illness in November 1936 the patient had noted a firm, nontender mass the size of "the end of a thumb" in the left side of her neck, and soon afterward similar masses had been felt in the same region and in the left axilla. These masses had fluctuated in size but had been enlarging for the preceding two months. The patient had not given this history at the time of her first visit in November 1937 because she considered it of no significance. During the preceding year she had noticed thickening, dryness and slight darkening of her skin, a loss of 20 pounds (9 Kg.), and increasing fatigability and nervousness. There had been no return of the menses following parturition.

She was admitted to the hospital March 8, 1939. The temperature was 37 C. (98.6 F.), pulse rate 110, respiratory rate

midlung field. Biopsy of a cervical lymph node revealed the histopathologic picture of Hodgkin's disease. Cultures of this node were sterile.

The patient was followed at short intervals until readmission to the hospital was possible. Administration of sulfapyridine, started on April 26, was attended by nausea and occasional vomiting. No change occurred in the size of the enlarged lymph nodes up to the time of readmission on May 7. Fever was absent during this period. A repeated roentgenogram of the chest on May 8 showed a slight decrease in the size of the densities in the right midlung field. On May 9 an elevation of temperature to 38 C. (100.4 F.) occurred and the patient complained of soreness of the mouth. Over the gums, buccal surfaces and hard palate were numerous irregularly outlined, white, adherent patches of exudate surrounded by hyperemic mucosa and measuring from 1 mm. to 1 cm. in diameter. The anterior pillars were reddened, but no lesions were noted in the pharynx. Cultures taken of material from the oral lesions yielded *Streptococcus viridans*, *Neisseria sicca* and *Brucella melitensis* var. *melitensis*. There was no growth on Sabouraud's medium and no spirochetes were seen on dark field examination of material from the lesions. *Brucella melitensis* var. *melitensis* was isolated from blood cultures at this time. The patient's temperature did not rise above 38.3 C. (100.9 F.). On May 11 a transfusion of 500 cc. of blood was given, the donor of which had *Brucella* agglutinins in high titer. On the following day the patient became afebrile and sulfapyridine, refused by the patient for the preceding two days, was resumed. The oral lesions disappeared in eight days and progressive diminution

in the size of the lymph nodes was noted. Blood cultures became sterile and the patient was discharged much improved on May 21. Sulfapyridine was continued for five days.

The patient returned on June 20 complaining of weakness and severe pruritus. It was thought that there had been an increase in the size of the cervical and left axillary nodes. She was readmitted to the hospital July 18, complaining of further enlargement of the lymph nodes, severe pruritus and weakness. She had had no known fever, and no loss of weight had occurred. For the preceding two weeks she had had a nonproductive, paroxysmal cough when lying on her back and a feeling of "tightness" on swallowing.

The temperature at this time was 37.8 C. (100 F.), pulse 80 and respiratory rate 20. The patient appeared chronically ill. Numerous discrete, firm, nontender lymph nodes from 1 to 2 cm. in diameter filled the left anterior and posterior cervical regions. Single nodes of similar size were felt in the submental region and above the suprasternal notch. A few small cervical nodes were felt on the right. In the left axilla a large mass of variously sized nodes measured 8 by 8 cm. The right axillary, epitrochlear and inguinal nodes were slightly enlarged. Examination of the heart and lungs was not remarkable. The firm, nontender liver edge was felt 3 cm. below the costal margin; the spleen was not felt.

A blood count revealed hemoglobin 72 per cent, red blood cells 3,320,000, white blood cells 18,800, polymorphonuclears 88 per cent (stab cells 11 per cent, juveniles 1 per cent), eosinophils 1 per cent, basophils 0, large lymphocytes 2 per cent, small lymphocytes 5 per cent and monocytes 4 per cent. A roentgenogram of the chest showed extensive mediastinal and hilar enlargement. Biopsy of a cervical node showed the characteristic signs of Hodgkin's disease; cultures of the node were sterile. Biopsy of the skin showed no definite lesions.

During the first week of the patient's hospital stay there was a daily elevation of temperature to 38.6 C. (101.5 F.), thereafter to 39.4 C. (102.9 F.). On July 22 sulfapyridine was started but had to be discontinued because of nausea and vomiting. Fifty cc. of bovine antimelitensis serum was given intravenously on August 2. On August 3 roentgen therapy to the cervical, mediastinal and upper abdominal regions was started. Her condition was unchanged at the time of discharge on August 10, but subsequently there was a marked decrease in the size of the cervical nodes and subsidence of cough.

The patient has returned for reexamination at intervals of from four to six weeks. Superficial enlargement of the lymph nodes and mediastinal enlargement have been recurrent, and areas of infiltration into the lungs have been demonstrable roentgenologically. Intermittent fever, cough and fatigability have continued. Under roentgen therapy there has been slight temporary improvement in her general condition.

This case is of interest because of the long duration of the disease with a tendency toward localization of the involvement of the lymph nodes. A clinical picture developed indistinguishable from acute brucellosis, and *Brucella melitensis* var. *melitensis* was isolated from blood and oral lesions. Coincidentally there were further enlargement of the lymph nodes and intensified pruritus. Although the stomatitis cleared and blood cultures became negative under treatment with sulfapyridine and immunotransfusion, the patient's general condition became worse and there was rapid and widespread progression of the Hodgkin's disease process.

CASE 8.—Cervical lymph node enlargement of two years' duration; isolation of *Brucella melitensis* var. *suis* from blood and lymph node cultures; treatment with sulfapyridine and immune serum; death three years after onset.

E. D., a Negro boy aged 6 years, was brought to the hospital on April 26, 1938, because of swelling in the right side of the neck of two years' duration. This enlargement of the neck was progressive and associated with intermittent fever of unknown degree. Several weeks before entry increasing weakness, pallidation and shortness of breath developed.

On physical examination the temperature was 39 C. (102 F.), pulse rate 120 and respiratory rate 28. The patient was weak and undernourished but in no acute distress. An enormous S shaped mass filled the entire right cervical region extending 25 cm. from below the ear over the clavicle and onto the shoulder and anterior wall of the chest. This mass was composed of firm, nontender lymph nodes measuring up to 5 cm. in diameter. A similar mass was felt in the left supraclavicular region, measuring about 8 cm. in diameter. There was no other lymph node enlargement. Examination of the chest was not remarkable. The liver was not palpable. The spleen was felt 5 cm. below the costal margin. There was slight edema of the ankles.

The Wassermann and Kahn reactions of the blood were negative; a blood count revealed hemoglobin 29 per cent, red blood cells 1,840,000, white blood cells 3,480, polymorphonuclears 74 per cent, eosinophils 1 per cent, large lymphocytes 4 per cent, small lymphocytes 13 per cent, monocytes 8 per cent. A roentgenogram of the chest showed marked tracheal displacement and a diffuse shadow extending out into the upper portion of the left lung field which could not be differentiated from displacement of the aorta. The enlarged mass in the neck obscured the right upper and middle lung fields. Biopsy of a cervical lymph node showed the histopathologic picture of Hodgkin's disease. *Brucella melitensis* var. *suis* was isolated

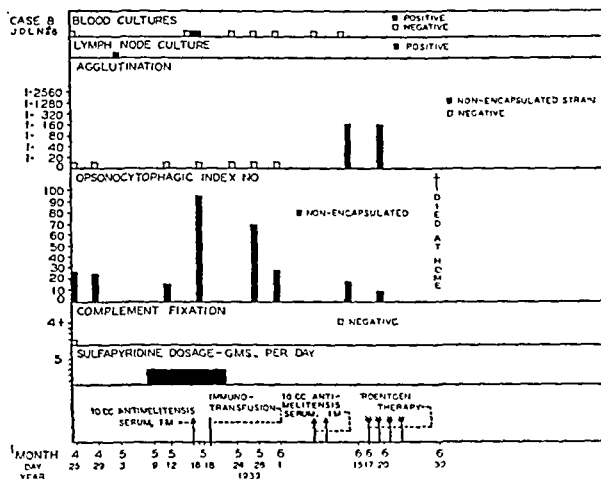


Chart 5.—Bacteriologic and immunologic studies in case 8.

from this node and from the blood. Immunologic studies are given in chart 5.

During the first four weeks of the patient's stay in the hospital there was irregular fever reaching 40.1 C. (104.2 F.). Repeated blood transfusions were given. Sulfapyridine was started on May 9 and discontinued on May 22 because of increasing leukopenia. Ten cc. of bovine antimelitensis serum was given intramuscularly on May 16. On May 19, following a blood transfusion from a donor found to have evidence of immunity to *Brucella* infection, the patient's temperature fell promptly and after remaining within normal limits for six days rose again. By May 25 a marked decrease in the size of the enlarged lymph nodes had occurred. Repeated injections of bovine antimelitensis serum on June 6 and June 8 were without demonstrable effect. Roentgen therapy to the cervical and mediastinal regions was started on June 17, resulting in a gradual diminution of fever but without further reduction in the size of the enlarged nodes. The patient appeared to be improved when discharged from the hospital on June 27 but he died quietly at home on June 30, 1939. Permission for necropsy was not obtained.

Treatment with sulfapyridine and immune serum apparently caused a marked reduction in the size of this patient's tremendously enlarged lymph nodes. There was no significant immune response to the *Brucella* infection.

CASE 9.—Intermittent fever; enlargement of the cervical and axillary lymph nodes on the left and hepatomegaly of three months' duration; *Brucella melitensis* var. *melitensis* isolated from blood cultures; treatment with sulfapyridine; recurrence of fever with icterus; treatment with antimelitensis serum; death one year after onset.

P. W., a man aged 29, a mulatto, admitted to the hospital on May 23, 1939, complained of weakness and swelling of the neck of three months' duration. His illness was considered to have started in the spring of 1939 with a gradual onset of anorexia, malaise, loss of weight and the appearance of painless swellings in the left side of the neck and in both axillae. There had been occasional bouts of high fever and recurrent generalized abdominal discomfort with dull aching pain in the lumbar region.

The temperature was 37.1 C. (98.8 F.), pulse 100, respiratory rate 20 and blood pressure 120 systolic and 70 diastolic. The patient was poorly nourished and appeared chronically ill. On the left side of the neck and in the left axilla there were large, firm, movable, nontender masses of lymph nodes measuring 5 by 3 cm. There was no other lymph node enlargement. Examination of the abdomen revealed marked voluntary muscle spasm. The liver extended 8 cm. below the right costal margin and was firm and tender. The spleen was not felt.

Wassermann and Kahn reactions were negative; a blood count revealed hemoglobin 52 per cent, red blood cells 3,490,000,

Sulfapyridine was started on June 24 and continued throughout the patient's hospital stay. Three days later the patient's temperature, previously within normal limits, rose to 40.2 C. (104.3 F.). The patient was febrile for seven days, after which his temperature fell by lysis. Coincident with the fall in temperature there was marked diminution in the size of the enlarged lymph nodes and liver and general improvement in the patient's clinical condition. He was much improved when discharged from the hospital on July 15.

He returned on July 21 complaining of a cutaneous eruption. Four days previously he had noticed a generalized erythematous eruption and pustular lesions in the region of the beard. The temperature was 37.5 C. (99.5 F.). There was a pustular eruption in the beard area and a generalized erythematous eruption with ecchymotic lesions over the distal portions of the extremities. Other physical conditions were unchanged. A blood count revealed hemoglobin 67 per cent, red blood cells 3,120,000, white blood cells 26,200, polymorphonuclears 42 per cent (stab cells 7 per cent), eosinophils 1 per cent, large lymphocytes 7 per cent, small lymphocytes 23 per cent, monocytes 7 per cent and lymphoblasts 19 per cent. It was considered that the patient had a toxic erythema due probably to sulfapyridine.

The patient returned on July 26 saying that the cutaneous eruption had subsided rapidly. But on the evening of the day of his preceding visit generalized abdominal pain and a severe watery diarrhea developed. He had had fever and slight nausea.

He vomited the morning of the day before admission and a dull, aching pain and extreme soreness in the right upper quadrant developed.

The temperature was 39.8 C. (103.6 F.), pulse rate 120 and respiratory rate 22. The scleras were slightly icteric. A few small, firm lymph nodes were felt in the cervical and left axillary regions. In the right axilla there was a large mass of recently enlarged nodes, each about 1 cm. in diameter. No epitrochlear nodes were felt. The inguinal nodes were barely palpable. The heart and lungs were not remarkable. There was rigidity, exquisite tenderness and rebound tenderness in the right upper quadrant of the abdomen. Elsewhere there was no muscle spasm or tenderness. The liver could not be palpated because of muscular rigidity. The spleen was not felt. No masses were felt. Rectal examination gave negative results.

The white blood cells numbered 8,700, polymorphonuclears 74 per cent (stab cells 5 per cent), eosinophils 0, basophils 0, large lymphocytes 5 per cent, small lymphocytes 16 per cent and monocytes 5 per cent. The van den Bergh reaction was direct; serum bilirubin was 3.8 mg. per hundred cubic centimeters.

The condition was considered related to abdominal Hodgkin's disease and the patient was admitted for observation. The day following entry the abdominal signs disappeared. He remained acutely ill with daily elevations of temperature to 40 C. (104 F.) until August 15, at which time he became afebrile and a rapid and marked improvement in his general condition followed. Fifty cc. of bovine antimelitensis serum was given intravenously on August 8. By the time of discharge, August 18, jaundice had disappeared, the enlarged lymph nodes had decreased in size and the spleen and liver were not felt.

The patient was readmitted to the hospital on December 11. In the interval weakness had been progressive and he had had intermittent fever and pain in the right upper quadrant.

The temperature was 38.2 C. (100.7 F.), pulse rate 116 and respiratory rate 30. The patient was pale and extremely emaciated and appeared gravely ill. There was slight icterus of the scleras. The left cervical and axillary nodes were firm, nontender and from 2 to 3 cm. in diameter. Expansion of the chest was poor. Over the right posterior part of the chest there was a palpable and audible friction fremitus with impairment of the percussion note and diminished breath and voice sounds. A systolic murmur was heard over the precordium. The abdomen was distended and the liver dullness extended

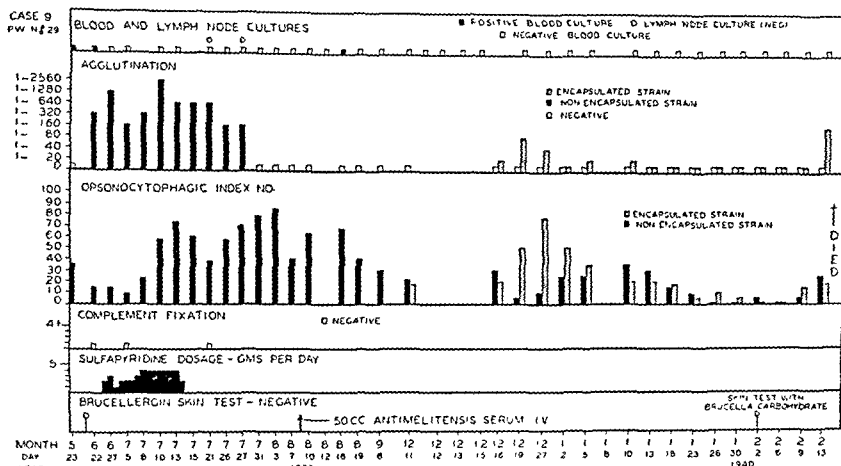


Chart 6.—Bacteriologic and immunologic studies in case 9.

white blood cells 6,700, polymorphonuclears 85 per cent (stab cells 23 per cent), eosinophils 0, basophils 0, large lymphocytes 2 per cent, small lymphocytes 4 per cent, monocytes 9 per cent. A roentgenogram of the chest showed moderately dense masses at the pulmonary hili which were considered to be enlarged lymph nodes. Bacteriologic and immunologic studies are given in chart 6.

The patient returned May 30, saying that he had had a mild infection of the upper respiratory tract and believed that he had had intermittent fever. The temperature was 39.7 C. (103.4 F.), pulse 112, respiratory rate 24. There was no significant change in the physical examination.

He was admitted to the hospital on June 21. In the interval he had continued to have intermittent fever, malaise and progressive loss of weight.

The temperature was 37.4 C. (99.3 F.), pulse 86, respiratory rate 20 and blood pressure 118 systolic and 74 diastolic. There was no change in the physical condition except for marked enlargement of the right axillary lymph nodes.

A blood count revealed hemoglobin 73 per cent, red blood cells 3,920,000, white blood cells 8,200, polymorphonuclears 79 per cent (stab cells 7 per cent), eosinophils 0, basophils 1 per cent, large lymphocytes 6 per cent, small lymphocytes 12 per cent, monocytes 2 per cent. A roentgenogram of the chest showed no change. A roentgenogram of the abdomen showed that the liver extended to the iliac crest. Biopsy of a cervical node revealed the histopathologic changes of Hodgkin's disease; node cultures were sterile.

to the level of the umbilicus. The spleen was palpable at the costal margin.

A blood count revealed hemoglobin 24 per cent, red blood cells 1,600,000, white blood cells 5,160 with polymorphonuclears 77 per cent (stab cells 5 per cent, juveniles 2 per cent), eosinophils 2 per cent, basophils 0, large lymphocytes 6 per cent, small lymphocytes 7 per cent, monocytes 8 per cent; urine and stool examinations gave negative results; the van den Bergh reaction was direct; plasma bilirubin was 1.4 mg. per hundred cubic centimeters. A roentgenogram of the chest showed the right lung obscured. The patient's course was characterized by fever, reaching 40 C. (104 F.) and progressive cachexia. Treatment was entirely symptomatic. Death occurred on Feb. 14, 1940.

Necropsy showed Hodgkin's disease involving the spleen, liver, adrenals, kidneys, bone marrow and lymph nodes, with compression of the common duct and partial obstruction. From necropsy cultures taken in triplicate *Brucella melitensis* var. *melitensis* was isolated from the liver and spleen. Diphtheroids were isolated from a mediastinal node.

Coincident with this patient's initial clinical improvement under sulfapyridine therapy was the appearance of serum agglutinins and increased phagocytosis. Phagocytosis was maintained during a succeeding febrile episode, but all evidence of an immune response was lacking during the terminal phase of the disease.

CASE 10.—C. B., a Negro woman aged 35, who entered the hospital on June 19, 1939, began in January 1939 to have painless, progressive enlargement of the left axillary lymph nodes, malaise and loss of weight. For six weeks preceding entry she had had fever. A firm, nontender, left cervical node, about 2 cm. in diameter, and a left axillary node, about 6 cm. in diameter, were palpable. Biopsy of an axillary node from the left side showed the histopathologic signs of Hodgkin's disease. Cultures taken of the nodes were sterile. *Brucella melitensis* var. *melitensis* was isolated from a blood culture taken on entry. The patient was febrile throughout her hospital stay and there was no significant improvement under treatment with sulfapyridine and bovine antimelitensis serum or roentgen therapy. Following discharge on August 12 febrile episodes continued, anemia became marked and death occurred in December. Permission for necropsy was not obtained.

CASE 11.—A. A., a white woman aged 40, admitted to the hospital on June 27, 1939, complained of weakness, loss of weight and enlargement of the neck of seven months' duration. Above the suprasternal notch and in the right cervical region were firm, nontender masses of enlarged lymph nodes measuring 5 by 4 cm. The spleen was palpable at the costal margin. A roentgenogram of the chest showed a large mediastinal mass. Biopsy of a cervical lymph node confirmed the diagnosis of Hodgkin's disease, and culture taken of this node and blood culture yielded *Brucella melitensis* var. *suis*. There was a moderate decrease in the size of the cervical and mediastinal lymph nodes under roentgen therapy.

CASE 12.—W. H., a Negro aged 64, admitted to the hospital July 7, 1939, complained of enlargement of the neck of six months' duration. In January 1939 the patient noted a nontender mass beneath the angle of the right jaw. Gradually numerous firm, nontender nodules appeared in both cervical regions which increased to a size sufficient to cause difficulty in rotating the neck. Transient regression of this enlargement had been noted. At the time of entry the anterior and posterior cervical lymph nodes were markedly enlarged, firm and nontender and measured from 1 to 3 cm. in diameter; the epitrochlear and inguinal nodes were barely palpable. Biopsy of a cervical lymph node showed the histopathologic signs of Hodgkin's disease. Cultures of the nodes were sterile. Roentgen therapy was given over the cervical region with prompt regression of enlargement of the lymph nodes, which has not recurred. On October 27, *Brucella melitensis* var. *suis* was isolated from a blood culture.

CASE 13.—W. M., a white man aged 37, who entered the hospital Nov. 16, 1939, began to be ill in the summer of 1936 with fatigability, loss of weight and pruritus. In September 1937 painless, slight enlargement of several cervical and inguinal lymph nodes was noted, and biopsy established the diagnosis

of Hodgkin's disease. In January 1938 enlargement of cervical, axillary and inguinal lymph nodes was noted and a roentgenogram of the chest showed widening of the mediastinum. Fever was present at this time. Under roentgen therapy the size of the lymph nodes regressed, fever subsided and the patient's general condition improved. There was subsequent recurrent enlargement of various groups of superficial lymph nodes which regressed promptly under roentgen therapy. The patient was relatively well until June 1939, when daily elevation of temperature and marked fatigability became established, but there was no recurrence of enlargement of the lymph nodes. *Brucella melitensis* var. *melitensis* was isolated from blood cultures taken on entry to the hospital. Under treatment with sulfanilamide and rabbit antimelitensis serum the patient became afebrile and gained in weight. Subsequently fever returned and a flaccid paralysis of the lower extremities developed with a sensory level at the eighth thoracic segment. Since this time his course has been characterized by fever and progressive cachexia.

CASE 14.—*Intermittent cervical lymph node enlargement regressing under roentgen therapy; hilar lymph node enlargement, fever and development of hepatosplenomegaly with ascites; death seven years after onset; Brucella melitensis* var. *suis* isolated in cultures taken post mortem of liver, spleen and peritoneal fluid.

G. B., a Jewish boy aged 13 years, who entered the hospital on Jan. 24, 1940, began to be ill in the spring of 1933 with enlargement of a left cervical lymph node, which subsided promptly after roentgen therapy. In July 1933 there had been recurrent enlargement of the lymph nodes in the same region, which again regressed after roentgen therapy but recurred in several months. In April 1936 biopsy of a cervical lymph node showed the histopathologic signs of Hodgkin's disease. The patient had no systemic symptoms until the fall of 1938, when fever, anorexia, marked fatigability and a dull aching pain developed in the upper

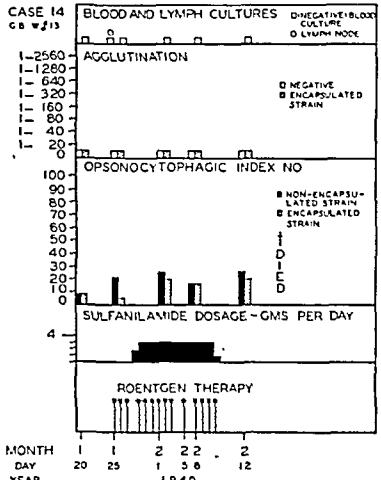


Chart 7.—Bacteriologic and immunologic studies in case 14.

part of the abdomen. At this time tachycardia, splenic enlargement and slight anemia were noted. In January 1939 a roentgenogram of the chest showed large hilar masses. Roentgen therapy was given over the chest and abdomen with temporary improvement. In July 1939 the patient was given sulfanilamide for one week, during which time the spleen decreased in size and improvement of anemia was noted but weakness continued. In November marked dyspnea developed on exertion with cyanosis and loud wheezing, which subsided after roentgen therapy over the mediastinum and upper part of the abdomen. The liver and spleen were palpable at this time and ascites was slowly accumulating. A daily elevation of temperature to 39 C. (102.2 F.) became established and loss of weight, weakness and anemia increased.

The temperature was 38.1 C. (100.6 F.), the pulse rate 130, respiratory rate 32 and blood pressure 120 systolic, 74 diastolic. The patient was pale and emaciated and appeared chronically ill. On the left side single, firm, nontender, cervical and axillary lymph nodes, about 2 cm. in diameter, were felt, as well as many smaller supraclavicular nodes. The inguinal nodes were barely palpable. The chest expanded poorly and there was dullness to flatness posteriorly on the left below the level of the sixth thoracic spine and anteriorly below the level of the fifth rib. The breath and voice sounds were diminished to absent over this area. The heart was enlarged and a systolic murmur was heard over the apex, which was transmitted to

the base. The abdomen was distended and there was shifting dullness in the flanks and a frank fluid wave. The liver edge was felt 9 cm. below the costal margin, firm and nontender. The spleen was felt 14 cm. below the costal margin, firm and moderately tender. Large external hemorrhoids were present. There was slight pitting edema over the dorsum of both feet.

Wassermann and Kahn reactions were negative; hemoglobin was 54 per cent, red blood cells numbered 2,850,000 and white blood cells 7,800, with polymorphonuclears 89 per cent (stab cells 1 per cent), eosinophils 0, basophils 0, large lymphocytes 0, small lymphocytes 5 per cent and monocytes 6 per cent. A roentgenogram of the chest revealed a shadow of uniform density over the lower left lung field and exaggerated hilar markings. Biopsy of a lymph node showed the histopathologic changes of Hodgkin's disease. Cultures taken of the nodes were sterile. Bacteriologic and immunologic studies are given in chart 7.

During the first week in the hospital the patient's temperature varied between 37.6 and 39.9 C. (99.5 and 103.8 F.); thereafter it gradually became lower and did not rise above 38 C. (100.4 F.). Roentgen therapy was given over the spleen, upper part of the abdomen and long bones. Repeated transfusions were given and iron and liver extract were administered, but anemia was progressive. On the fifth hospital day sulfanilamide was started in small doses. The patient became progressively weaker, increasing anemia rapidly developed and death occurred on February 18.

Necropsy showed Hodgkin's disease involving the spleen, liver, diaphragm, pleuras, adrenals and all lymph nodes. *Brucella melitensis* var. suis and diphtheroids were isolated from triplicate cultures taken of material from the spleen, liver and peritoneal fluid at necropsy. Diphtheroids were also isolated from a mesenteric lymph node.

During the terminal phase of this patient's disease there was no evidence of an immune response toward the *Brucella* infection which was shown to exist at necropsy.

COMMENT

The demonstration of *Brucella* infection in fourteen consecutive cases of Hodgkin's disease raises questions that can be answered only by further investigation. The obvious question may be raised as to whether the isolation of this organism from patients with Hodgkin's disease represents merely latent *Brucella* infection or whether it may be of etiologic significance. It is true that the majority of these fourteen patients were natives of an area in which *Brucella* infection is widespread, but if our observations represent merely a latent infection peculiar to this region one should expect to obtain positive cultures with equal frequency from lymph nodes obtained from other patients suffering from chronic diseases involving the lymphatic system. Such has not been the case, despite repeated study of a much larger group of patients with diseases such as lymphosarcoma, leukemia, tuberculous adenitis and the like. *Brucella* has been isolated only once from cultures of sixty-seven lymph nodes removed from patients not suffering from Hodgkin's disease.² From such patients repeated blood cultures have been negative with one exception. On the other hand, *Brucella* has been isolated from blood or lymph nodes on culture, or from both, in these fourteen consecutive cases of Hodgkin's disease. Furthermore, cultures yielding *Brucella* have been obtained with the greatest frequency when Hodgkin's disease was actively progressing, rather than when it was subacute or temporarily arrested.

A sufficient correlation has been found to exist between the cultural and immunologic manifestations and the clinical course of these patients to justify the belief that the *Brucella* infection directly influences the syndrome of Hodgkin's disease. The frequent lack of all evidence of an immune response when *Brucella* could be isolated from blood cultures during recurrences of

Hodgkin's disease has been very striking. Maximum clinical improvement in these fourteen cases has coincided with the presence of serum agglutinins and significant degrees of phagocytosis for *Brucella*.

Although the observations reported here suggest the possible etiologic importance of *Brucella* in the Hodgkin's disease process, the rigid postulates of Koch have not been fulfilled. It has been possible to induce disease leading to death in guinea pigs and mice by intraperitoneal injection of blood or by a suspension of lymph nodes from patients with Hodgkin's disease and to recover *Brucella* subsequently from the blood or tissues of these animals, but lesions identical with those of Hodgkin's disease have not been observed. This phase of the problem is being investigated by the department of pathology and will be reported on later.

Treatment of these fourteen patients has been directed primarily toward the existing *Brucella* infection as a further means of studying the influence of such infection on the course of Hodgkin's disease. A definite and often striking decrease in the size of enlarged lymph nodes has been observed after administration of sulfanilamide or sulfapyridine. Immune serum therapy, utilizing whole blood or blood serum from persons recovered from brucellosis or having serum agglutinins in high titer, or a commercial antiserum, has been combined with sulfanilamide or sulfapyridine, but the effectiveness of these serums has not been demonstrated. Since recent investigations in this laboratory have shown that *Brucella* organisms isolated from many of the patients suffering from Hodgkin's disease possess capsules and show significant antigenic differences from the laboratory strains, further consideration must be given to the antibody properties of the serums used in the treatment of *Brucella* infections.

SUMMARY

The coexistence of *Brucella* infection and Hodgkin's disease has been demonstrated in fourteen consecutive cases by the isolation of *Brucella melitensis* from blood or lymph node cultures. *Brucella* has been isolated but once from blood or lymph node cultures from a much larger group suffering from diseases involving the lymph nodes other than those with Hodgkin's disease. Although the data in this study do not establish an etiologic relationship of *Brucella* to Hodgkin's disease, it is suggested that the clinical course of Hodgkin's disease may be significantly influenced by *Brucella* infection.

Circumventing Our Conflicts.—It may be profitable to examine briefly a few of the devices we tend to employ for the purpose of circumventing our conflicts. . . . Projection is a psychological expedient that seeks to circumvent the hard realities of our conflicts by shifting the blame we should accept ourselves upon others or upon the conditions of life. Projection is common, and in its milder exhibitions it is harmless enough. For instance, the batter strikes out, throws down his bat, and says that the umpire needs glasses; the college girl says that the professor must have looked over the papers very hastily or she would have been credited with a perfect paper; the housewife complains that the baking powder was inferior in quality or the biscuits would have risen. But if practiced too frequently and with too much facility, projection readily becomes a grave menace to the integrity of the personality and the peace of the mind. Soon it erects an impassable barrier between the individual and the possibility of seeing himself as he really is. The descent may be very rapid—excessive criticism, pessimism, sarcasm, cynicism, prejudice, intolerance, hatreds, brooding. And from here it is not a very long step into the territory of mental disease—ideas of reference, hallucinations, delusions of persecution.—Strecker, Edward A., *The Man and the Mob, Mental Hygiene* 24:529 (Oct.) 1940.

DIFFERENTIAL DIAGNOSIS OF VARIOUS
FORMS OF ENCEPHALITIS

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Sleeping sickness is not the only type of encephalitis. There are many other encephalitides, complexes which are not easily differentiated from one another, complexes which result from a combination of degenerative and disseminated inflammatory changes in the brain, spinal cord and meninges. The lesions of encephalitis are sometimes spotty and scattered, and sometimes generalized. At times the spread of the disease in the central nervous system may be slow and at other times rapid. Therefore diverse signs and symptoms are seen. An encephalitic condition may even have different stages, each stage presenting its own signs, signs which may be referable to the motor, sensory, reflex or autonomic systems and, from an anatomic standpoint, present cerebral, basal ganglionic, bulbar, spinal or meningeal symptoms.

CLASSIFICATION OF ENCEPHALITIDES

A. Encephalitides which occur secondary to or accompany some acute infection:

1. Cerebrospinal fever, chickenpox, dysentery, bacterial endocarditis, herpes zoster, malaria, measles, German measles, mumps, pneumonia, purpura, scarlet fever, puerperal sepsis, smallpox, syphilis, tonsillitis, tuberculosis, typhoid, typhus, undulant fever, whooping cough and any infectious disease of the brain.

2. Usually these include the hemorrhagic types of encephalitis.

B. Encephalitides which occur secondary to ingestion or injections of alcohol, benzene, carbon monoxide, arsenic, lead, thallium, bismuth and so on.

C. Encephalitides associated with poisonings.

D. Encephalitides, toxic neuropathies or encephalopathies (other than those following specific infections) (other synonyms: diffuse meningo-encephalomyelitis, multiple neuritis, toxic neuronitis, acute disseminated encephalomyelitis, dissociated encephalitis), possibly acute multiple sclerosis.

E. Encephalitides which accompany metabolic disorders, such as uremia and the toxemia of pregnancy.

F. Encephalitides associated with localized swellings inside the brain case, probably pressure or irritative phenomena: pachymeningitis, extradural abscess, fractures, and so on.

G. Encephalitides following injection of an active or passive immune principle: smallpox vaccine, rabies vaccine, antitoxins or antisera (tetanus, diphtheria).

H. Encephalitides caused by specific viruses (other than herpes zoster): Japanese type B encephalitis, St. Louis encephalitis, equine encephalomyelitis, possibly lethargic encephalitis, Australian X disease, polioencephalomyelitis, benign lymphocytic choriomeningitis.

I. Diseases or conditions which simulate encephalitis: caisson disease, convulsions, oculomotor lesions, purulent meningitis, neuroses, acute chorea and vascular lesions in the brain associated with embolus, thrombus or hemorrhage.

DIFFERENTIAL DIAGNOSIS

A. Most of these clinical conditions are easily recognized from the history. Those that are difficult to differentiate at times are St. Louis encephalitis, equine encephalomyelitis, Japanese type B encephalitis, polioencephalomyelitis, lethargic encephalitis, acute benign lymphocytic choriomeningitis, Australian X disease, Schilder's disease (sometimes), disseminated encephalomyelitis (or toxic neuronitis), acute multiple sclerosis as well as tuberculous and syphilitic meningitis. Some of these diseases are new to most physicians; some have appeared only in certain places, yet experience indicates that such localizations are never permanent and all physicians should be conscious of their existence.

B. Differential diagnosis is based on a consideration of (1) appearance, age, sex and fate of the patient; (2) temperature, pulse and respiratory rate; (3) history of the illness, especially as regards onset and chronology of symptoms; (4) neurologic changes; (5) spinal fluid manifestations; (6) results of immunologic tests in animals.

C. There are various types of lesions. Encephalitis usually involves the upper motor neuron; when this occurs, the signs are hyperactive deep tendon reflexes, loss of superficial abdominal reflexes, presence of pathologic reflexes (Babinski, Oppenheim, Chaddock, Stone), spasticity, incoordination of muscles without loss of function, and a normal electrical reaction. Some patients may have one, some all and some none of these signs, despite the fact that the upper motor neuron is usually irritated. Often the signs are absent, and coma and a condition tantamount to cord shock with generalized flaccidity occur. The encephalitic condition may be combined with signs of a lower motor neuron lesion such as flaccidity, diminished reflexes, loss of motor function, atrophy or reaction to degeneration, or a meningeal type of reaction may be produced with a positive Kernig and Brudzinski sign, stiff neck, opisthotonos and hyperactive reflexes.

1. Appearance, age, sex and fate of the patient: The appearance is not indicative, since any type of encephalitis may produce somnolence, choreiform movements, myoclonic spasms or tics. The swiftness and diffuseness of the spread will determine the appearance of the patient when he is first examined. In polioencephalomyelitis there is usually not much lethargy and the encephalitis does not persist long. In tuberculous meningitis the patient is apathetic at first and only after days of illness does he become somnolent and have choreiform or myoclonic movements. In benign lymphocytic choriomeningitis the patient is active. In St. Louis encephalitis he looks extremely ill and may appear somnolent unless the attack is an abortive one, in which case there may be no objective response. The same general remarks hold true for equine encephalomyelitis. Patients ill with Japanese type B encephalitis and Australian X disease may be apathetic or comatose. Patients ill with lethargic encephalitis may look irritable, stuporous or lethargic. Usually but few symptoms accompany the onset of Schilder's disease. Patients ill with disseminated encephalomyelitis and acute multiple sclerosis are usually mentally fit. In syphilitic meningitis the patients, who are usually in the older age groups, may or may not appear ill.

Equine encephalomyelitis, polioencephalomyelitis and Schilder's disease are more apt to occur in children. Fifty per cent of the cases of Australian X disease occur in children under 5 years of age. Japanese type B

and lethargic encephalitis usually are found in older age groups.

More males than females have Australian X disease, and twice as many males as females have Schilder's disease. Tuberculous meningitis occurs in any sex and at any age, most commonly, however, in childhood.

Lethargic encephalitis comes on in the winter and spring time; polioencephalomyelitis, St. Louis encephalitis, Japanese type B encephalitis and Australian X disease in the summer and early fall. (Australian X disease occurs during the summer months in the South-

encephalomyelitis, 66 per cent die. Cerebral irritation caused by poliomyelitis virus is not serious. It is only when this irritation is combined with a bulbar type of palsy that the mortality rises to from 50 to 90 per cent. From 25 to 40 per cent of those ill with lethargic encephalomyelitis die; in Japanese type B encephalitis, 60 per cent or more die; in Schilder's disease, 100 per cent die, death occurring suddenly or eventually as long as ten to twelve years after the initial onset.

2. Temperature, pulse, respiratory rate: Nothing is distinctive about the temperature reactions, although

TABLE 1.—General Information

Type of Disease	Age	Sex	Time	Locale	Mortality
Benign lymphocytic choriomeningitis.....	Any	Any	Any	Any	0
St. Louis encephalitis.....	Any	Any	Summer	In and near vicinity of St. Louis; along streams?	20%
Equine encephalomyelitis	Children mostly	Any	Summer	Where epizootic diseases occur in animals	70%
Japanese type B encephalitis.....	Older people	Any	Summer	Japan	60%
Polioencephalomyelitis	Children especially	Any	Summer	Any	70% with bulbar; 0-3% without
Lethargic encephalitis	3d-4th decade	Any	Winter and spring	Any	25-40%
Tuberculous meningitis	Young usually	Any	Any	Any with history of exposure	100%
Syphilitic meningitis	Usually older	Any	Any	Any	30%
Schilder's disease	Young usually	More males	Any	Any	100% eventually
Australian X disease	50% under 5 years of age	More males	Summer	Australia	70%
Acute disseminated encephalomyelitis and acute multiple sclerosis...	Any	Any	Any	Any	10%

TABLE 2.—General Information Continued

Type of Disease	Temperature	Pulse	Respirations	History	
				Onset	Progress
Benign lymphocytic choriomeningitis.....	High-moderate	Follows temperature	Follows temperature	Abrupt	Rapid
St. Louis encephalitis.....	High	Follows temperature	Follows temperature	Abrupt to 1-5 days	Rapid, usually
Equine encephalomyelitis	High	Follows temperature	Follows temperature	Abrupt	Rapid
Japanese type B encephalitis.....	High	Follows temperature	Follows temperature	Abrupt	Rapid
Polioencephalomyelitis ..	Either high or low	Normal or fast	Normal or slow and deep	Abrupt or camel type	Rapid, usually
Lethargic encephalitis	Moderate, occasionally high	Follows temperature	Follows temperature	Abrupt	Variable, slow or rapid
Tuberculous meningitis	Normal, then high	Follows temperature	Irregular or Biot's type	Gradual	Rapid at end
Syphilitic meningitis	Normal or slightly increased	Follows temperature	Follows temperature	Abrupt or gradual	Slow
Schilder's disease	Low	Not abnormal	Not abnormal until end	Slow	Variable
Australian X disease ...	High	Follows temperature	Follows temperature	Abrupt	Rapid
Acute disseminated encephalomyelitis and acute multiple sclerosis	Low or high	Follows temperature	Follows temperature	Abrupt or gradual	Slow or rapid

ern hemisphere.) Tuberculous meningitis will happen during any season.

There may be a history of exposure in tuberculous meningitis and a history of an animal epizootic disease in equine encephalomyelitis. The locale suggests the diagnosis of Australian X, Japanese type B and St. Louis encephalitis.

Only rarely does a patient ill with tuberculous meningitis live; for practical purposes it can be said that the mortality rate is 100 per cent. Patients with benign lymphocytic choriomeningitis recover. The mortality in St. Louis encephalitis ranges from 17 to 22 per cent; in children under 15 years it is 5 per cent. In equine

in tuberculous meningitis there may not be any fever until after the patient has lapsed into somnolence.

A change in the character of the pulse usually depends on the amount of fever, but it may also be influenced by increased pressure on the structures at the base of the brain or by inflammatory involvement of the vagus. Infiltration of the vagus and sixth nerves can be demonstrated in tuberculous meningitis. Biot's type of respiration, alternating apnea and hyperpnea may be produced by increased pressure. When the vagal nerve nuclei are involved, as they are in bulbar polioencephalomyelitis, vagus escapement is the result and a tachycardia together with a slowed but deepened respiratory rate

develops; when there is a marked increase in basilar pressure the pulse may be slowed down.

3. History of illness, onset and chronology of symptoms: An abrupt onset is usually seen in all types of encephalitis save in those associated with tuberculous meningitis and Schilder's disease. The history in syphilitic meningitis is also variable. In tuberculous meningitis the history is almost pathognomonic, relatively asymptomatic at first, gradually progressing to the final

tically comatose and hence not very reactive. Late in the course of tuberculous meningitis, any and every type of neurologic reaction may be found. If there is evidence of an upper motor neuron lesion combined with evidence of a lower motor neuron lesion the latter condition is ignored and a diagnosis of an encephalitis is made unless the paralysis or the lower motor neuron type of lesion is segmental in type, in which case poliomyelitis should be diagnosed.

TABLE 3.—Spinal Fluid Manifestations

Type of Disease	Color	Cells		Pressure	Organisms	Globulin	Sugar	Chlorides
		Number	Type					
Benign lymphocytic choriomeningitis.....	Clear to opaque	100 to 3,000	Lymphocyte	+	—	±	—	No significance
St. Louis encephalitis.....	Clear	50 to 1,000	Lymphocyte	+	—	+	±	No significance
Equine encephalomyelitis	Clear-ground glass	200 to 2,000	Leukocyte	±	—	++++	—	No significance
Japanese type B encephalitis.....	Clear	100	Lymphocyte	±	—	+	—	No significance
Polioencephalomyelitis	Clear	20 to 1,000	Lymphocyte may be leukocyte at first	±	—	+	—	No significance
Lethargic encephalitis	Clear	100 to 200	Lymphocyte	±	—	+	—	No significance
Tuberculous meningitis	Clear to faintly opaque	30 to 1,000 usually under 100	Lymphocyte may be leukocyte at first	±	+	+++	Decreased	Decreased
Syphilitic meningitis	Clear	Normal to 500	Lymphocyte	±	—	++	—	No significance
Schilder's disease	Clear	Normal	Normal	—	—	—	—	No significance
Australian X disease.....	Clear	100	Lymphocyte	±	—	+	—	No significance
Acute disseminated encephalomyelitis and acute multiple sclerosis	Clear	Normal or slight increase	Negative or lymphocyte	—	—	+	—	No significance

TABLE 4.—General Objective Symptoms

Type of Disease *	Muscle Pain	Upper Motor Neuron Reflexes	Spastic Plegias	Lower Motor Neuron Reflexes	Flaccid Plegias	Meningeal	Somnolent or Drowsy or Comatose	Psychic, Maniacal, Irritable, Memory, Orientation, Attention, Understanding Poor	Myoclonic Movements, Choreiform Movements, Tremors, Twitchings, Irritations, Hyperkinetic	Ocular				Vertigo
										Nystagmus	Muscle Paralysis	Optic Nerve Involvement	Other Cranial Nerves	
Benign lymphocytic choriomeningitis.....	—	—	—	—	—	+	+	—	—	—	—	—	—	—
St. Louis encephalitis.....	—	+	+	—	—	±	+	+	+	—	—	—	—?	+
Equine encephalitis	—	+	—	—	+	±	+	+	—	—?	—?	—	7th	—
Japanese type B encephalitis.....	—	±	—	—	—	±	+	+	—	—	—	—	—	—
Polioencephalomyelitis	+	—	—	+	+	+	±	—	±	±	±	—	Anyone	—
Lethargic encephalitis	—	+	±	—	±	+	+	+	+	+	+	±	Others	+
Tuberculous meningitis	±	+	+	+	+	+	+	—	±	+	+	±	Others	+
Syphilitic meningitis	—	—	—	—	±	±	±	±	±	±	+	±	±	—
Schilder's disease	+	+	+	—	±	—	—	+	+	—	—	±?	—	—
Australian X disease.....	—	+	±	—	—	±	+	+	+	—	—	—	±	—
Acute disseminated encephalomyelitis and acute multiple sclerosis.....	+	±	—	+	+	±	—	—	±	—	±	+	Others	—

* Of course, patients do not appear comatose and maniacal simultaneously. The plus sign merely indicates that such a condition is possible at some time or another. A plus minus sign indicates that the condition may be present, although usually not.

stage over a period of from seven to twenty-one days. Schilder's disease often extends over a long period of time.

4. Neurologic observations: These are not always helpful, since the nervous system reacts only in certain ways, regardless of the stimulus. One should first ascertain whether an upper motor neuron lesion is present. Theoretically an encephalitis patient should have an upper motor neuron response, but many of the encephalitides so shock the patient, especially in equine encephalomyelitis, as to render him somnolent or prac-

Save for infants under 6 months of age, who rarely show objective neurologic phenomena, signs of meningeal irritation are often present with the various encephalitides. In children the only evidence that there may be trouble is when convulsions, high fever, coma and a bulging fontanel are present.

In the acute stages the Queckenstedt maneuver and the eyeground examination are of little practical value in differential diagnosis save in syphilitic meningitis, in which there may be a neuritis and atrophy. The eye muscles are rarely involved in St. Louis enceph-

litis, Australian X disease, Japanese type B encephalitis and lymphocytic choriomeningitis, although vision may be blurred in the latter. The optic muscles are nearly always involved in lethargic encephalitis, eventually always in tuberculous meningitis and at times in polioencephalomyelitis and syphilitic meningitis.

5. Spinal fluid observations: Any acute infection which causes a pyogenic response is ruled out if lymphocytes are found in the spinal fluid. When an abscess is deeply placed in the brain substance, the cellular reaction in the spinal fluid may first be lymphocytic, the type of cell changing to a polymorphonuclear leukocyte as the mass nears the brain surface. When there is an increase in the number of lymphocytes in the spinal fluid, the patient has some one of the encephalitis or tuberculous or syphilitic meningitis. If the spinal fluid contains 40 per cent or more of lymphocytes, the chances are that the true cellular response will eventually be a lymphocytic increase. During the first day or so after the onset of tuberculous meningitis, the cells found may be chiefly polymorphonuclear leukocytes. There is a change, however, within twenty-four

disease. There may be from a few to a few hundred cells in syphilitic meningitis.

The more protein present in the spinal fluid, the more severe the disease. Compared to the number of cells in lymphocytic choriomeningitis but little protein is found, and that is usually due to nucleoproteins, since filtering out the cells seems to remove it. A relatively small amount is present in lethargic encephalitis, definitely more in equine encephalomyelitis, Japanese type B encephalitis and St. Louis encephalitis, and a goodly quantity in tuberculous meningitis. In acute disseminated encephalomyelitis (and acute multiple sclerosis) there is nearly always a slight or a moderate amount of protein and few or, more often, no cells.

The spinal fluid Wassermann reaction will be positive in syphilitic meningitis and a syphilitic colloidal gold curve produced.

The sugar content is slightly increased in cases of epidemic encephalitis; it is definitely decreased in tuberculous meningitis.

6. Immunologic tests: There are only two ways to identify disease beyond a doubt: (1) by isolating the causative factor in the central nervous system and (2), if the patient recovers, by demonstrating that he has specific neutralizing antibodies in the blood serum. Isolation of the virus factor has occurred in lymphocytic choriomeningitis, St. Louis encephalitis, Japanese type B encephalitis, Australian X disease, equine encephalomyelitis and poliomyelitis. Specific neutralizing antibodies are present in the same diseases. No virus has ever been isolated in lethargic encephalitis, disseminated encephalomyelitis or acute multiple sclerosis.

CONCLUSIONS

If a patient has a disease of sudden onset and a spinal fluid containing but little protein and a great many cells, practically all of which are lymphocytes, and he begins to get well within a few days and there are no sequelae, the diagnosis may be lymphocytic choriomeningitis or abortive poliomyelitis.

If during the summer, in a community where horses, pigeons and other animals are dying of an epizootic disease, a patient develops a disease the onset of which is sudden and explosive in type, accompanied by high fever, not too obvious neurologic symptoms and from 200 to 2,000 cells, practically all polymorphonuclear leukocytes, and no organisms in the spinal fluid, the diagnosis is probably equine encephalomyelitis.

If during the summer a patient has signs similar to those of equine encephalomyelitis but with a lymphocytic count in the spinal fluid, then, dependent on the location, Japanese encephalitis, St. Louis encephalomyelitis or Australian X disease may be considered.

If the patient has a disease with a gradual onset, at first with little or no fever, and he slowly but inexorably becomes worse over a period of from seven to twenty-one days, the disease going on to a somnolent or encephalitic condition, at which time fever appears, and if at this time there are bizarre neurologic signs and an increase in the number of cells in the spinal fluid practically all of which are lymphocytes, the diagnosis is probably tuberculous meningitis. Guinea pig inoculations confirm this as well as demonstrating the presence of the organism.

If during the winter, fall or spring the disease starts suddenly with signs of an upper motor neuron lesion, such as a tic, nystagmus, double vision, absent abdomi-

TABLE 5.—Immunologic Data

Type of Disease	Isolation of Virus from the Central Nervous System	Neutralization of Virus with Specific Antiserum	Reproduction of Disease in Animals
Benign lymphocytic choriomeningitis	+	+	+
St. Louis encephalitis	+	+	+
Equine encephalomyelitis	+	+	+
Japanese type B encephalitis	+	+	+
Polioencephalomyelitis	+	+	+
Lethargic encephalitis	—	—	—
Tuberculous meningitis	Organisms can be isolated	—	—
Syphilitic meningitis	Wassermann positive	—	—
Schilder's disease	—	—	—
Australian X disease	+	+	+
Acute disseminated encephalomyelitis and acute multiple sclerosis..	—	—	—

to forty-eight hours and the cells then become permanently and predominantly lymphocytes. The chances that a lumbar puncture would be done early enough in the disease to catch such a reaction are very slight and by the time the patient has reached the stage of somnolence the cells are practically always lymphocytic in type. The predominant cells in the first stages of equine encephalomyelitis and polioencephalomyelitis may also be polymorphonuclear leukocytes. In the latter instance, these change to lymphocytes within twenty-four to forty-eight hours. The change seems to occur so slowly, however, in equine encephalomyelitis that the patient may die before this happens. If the predominant cells are lymphocytes, as they usually are by the time the practitioner sees them, the patient has one of the diseases under discussion, Schilder's disease, acute multiple sclerosis and disseminated encephalomyelitis excepted.

The total number of cells in the spinal fluid varies. In lethargic encephalitis there may be no cells to a hundred, usually from thirty to fifty; in lymphocytic choriomeningitis, as in equine encephalomyelitis, Japanese type B encephalitis and Australian X disease, there may be as high as a few thousand. In tuberculous meningitis the cell count is low, the average being less than 100, although at times it may be as high as from 500 to 1,000. There is no cellular reaction in Schilder's

nal reflexes and hyperactive deep reflexes or even pathologic reflexes, and if the spinal fluid contains some protein and but a slightly increased number of cells, all of which are lymphocytes, the diagnosis is probably lethargic encephalitis.

If the disease starts slowly and extends slowly and the patient shows signs of disturbed vision, spastic paralysis and mental retardation, Schilder's disease should be considered.

If all the signs of an encephalitis appear and yet there are segmental palsies of a lower motor neuron type in the muscles of the arms or legs, the diagnosis is poliomyelitis.

If the patient develops spotty signs of motor and sensory involvement, especially a dissociated appreciation of pain and temperature sensation, and paralysis with bizarre reflex responses, and the spinal fluid contains few or no cells and an increased amount of protein, the patient probably has disseminated encephalomyelitis. Such a syndrome cannot be differentiated from acute multiple sclerosis at this stage. If the patient recovers and has recurrences, multiple sclerosis is thought of; if he remains permanently cured, disseminated encephalomyelitis is considered.

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Clinical Notes, Suggestions and New Instruments

USE OF CELLOPHANE CYLINDERS FOR DESICCATING BLOOD PLASMA

A RAPID, ECONOMICAL AND BACTERIOLOGICALLY SAFE METHOD

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DETROIT

The present day use of blood banks and the tendency toward the use of stored blood and blood plasma have emphasized the importance of methods for preserving the plasma. At constant low temperatures liquid plasma may be stored safely for a number of months, but such conditions are difficult and expensive to maintain. Storage of large quantities of liquid under these exacting conditions is best accomplished only in stationary units, so that the mobility necessary for military or other emergency uses presents further expensive obstacles.

As pointed out by Flosdorf and Mudd¹ in 1935, the desiccation of serum was successfully accomplished by C. Martin in 1896, by M. J. Rosenau in 1895, by Noguchi in 1907 and by Burrows and Cohn in 1918. But all these methods produced physico-chemical changes in the material and a poorly soluble end product. Shackell in 1909 first introduced the process of desiccation by means of freezing, vacuum and sulfuric acid. Reichel in 1932 improved the method of Shackell and was able to desiccate large quantities rapidly but had difficulty in handling the hygroscopic product.

Flosdorf and Mudd introduced a modification of Shackell's and Reichel's method by processing the serum in the original containers. They (1) secured automatic regulation of the temperature during processing, (2) completed dehydration within a reasonable time, (3) provided a practical means of sealing the containers without loss of vacuum and (4) preserved asepsis throughout the process.

In 1938 Flosdorf and Mudd² further improved their method by the addition of a chemical desiccant—anhydrous calcium sulfate, or "drierite"—and designated it the "cryochem-process."

From the Department of Laboratories, Henry Ford Hospital.

1. Flosdorf, E. W., and Mudd, Stuart: Procedure and Apparatus for Preservation in "Lyophil" Form of Serum and Other Biological Substances, *J. Immunology* 29: 389-425 (Nov.) 1935.

2. Flosdorf, E. W., and Mudd, Stuart: An Improved Procedure and Apparatus for Preservation of Sera, Micro-Organisms and Other Substances—the Cryochem-Process, *J. Immunology* 31: 469-490 (June) 1938.

Again in 1940 a purely mechanical method of desiccation with a high vacuum or "desivac process" was described by the same authors.³

As early as 1917 Phillip A. Kober⁴ demonstrated the great speed with which water vapor passed through collodion bags and called the process pervaporation, at the same time describing the process of perstillation and percrystallization, which also utilized collodion bags.

Kunitz and Simms⁵ in 1928 and Simms⁶ in 1930 described a concentrating dialyzer which consisted of collodion sacs under partial vacuum, using it also to concentrate fluid to small amounts while keeping it at a low temperature.

Morell and Schwartzman⁷ in 1937 used small cellophane bags to prepare and preserve bacterial products.

William Thalheimer⁸ in 1938 pointed out that cellophane bags could readily be made from cellophane tubing and could be sterilized in steam. He found that bags containing 1,000 cc. of filtered serum could be reduced by from 20 to 25 cc. an hour if suspended at room temperature in front of an electric fan, and almost as fast in the refrigerator. Further, it was pointed out that the concentrated serum could be regenerated by placing the bag in water.

Following the introduction of cellophane tubing as a substitute for rubber tubing in intravenous therapy,⁹ we noted the rapid concentration of whole blood hung up in these three-eighths inch diameter tubes with complete desiccation of 150 cc. in twelve hours at 70 F. This led to a review of the literature and further experimentation with lengths of three-eighths inch tubing and with 4½ inch tubing. The initial loss of water vapor from blood plasma from the tubes was rapid, especially when a fan was played on them; but the further the concentration proceeded the slower the process proved, so that from seventy-two to ninety-six hours were required to desiccate 400 cc. of plasma completely. Further, it was noted that in the latter part of the process an abundant gray precipitate was thrown down. The final product was a rubbery opaque mass which was only slowly soluble after being ground in a mortar. Once this product was dissolved, it began precipitating out again so that it was not suitable for intravenous injections into either animals or man.

Flosdorf and Mudd emphasized the rapidity of desiccation and the porous product obtained by their method; efforts to approach their results led us to devise the double walled cellophane cylinders (E in the illustration), sealed at each end, thus increasing the surface area 100 per cent and allowing for the circulation of air through the center as well as about the outside. The inner cylinder is made somewhat longer, so that filtered air may be introduced with the plasma. The ends are sealed with heavily tinned screw clamps (B and C). A metal bar (D) is soldered across the outer clamp so that the cylinder may be attached to the rotating mechanism. F shows the rotating unit consisting of two wheels, each 24 or more inches in diameter, mounted on a steel axle. Rotation is accomplished at 20 revolutions per minute by means of a small geared motor. Circulation of warm dry air is provided by a 16 inch electric fan (H) on which are mounted several electric strip heaters (G). On the rotor, which measures 24 inches in diameter, from twelve to eighteen cylinder units (E) 14 inches long and 4½ inches in diameter, each containing 300 cc. of plasma, may be attached. Thus 5,400 cc. of plasma may be desiccated at one time with the smallest unit.

The cellophane cylinders of larger size were furnished through the courtesy of the Visking Corporation of Chicago. These cylinders are dry and are thinly coated with glycerin. In the

3. Flosdorf, E. W.; Stokes, F. J., and Mudd, Stuart: The Desivac Process for Drying from the Frozen State, *J. A. M. A.* 115: 1095-1097 (Sept. 28) 1940.

4. Kober, P. A.: Pervaporation, Perstillation and Percrystallization, *J. Am. Chem. Soc.* 39: 944-948, 1917.

5. Kunitz, M., and Simms, H. S.: Dialysis with Stirring, *J. Gen. Physiol.* 11: 641-644, 1928.

6. Simms, H. S.: A Concentrating Dialyzer, *J. Exper. Med.* 51: 319-326 (Feb.) 1930.

7. Morell, Sam, and Schwartzman, Gregory: The Use of Dialysis in the Preparation and Purification of Immunologically Active Bacterial Products, *Science* 86: 130 (Aug. 6) 1937.

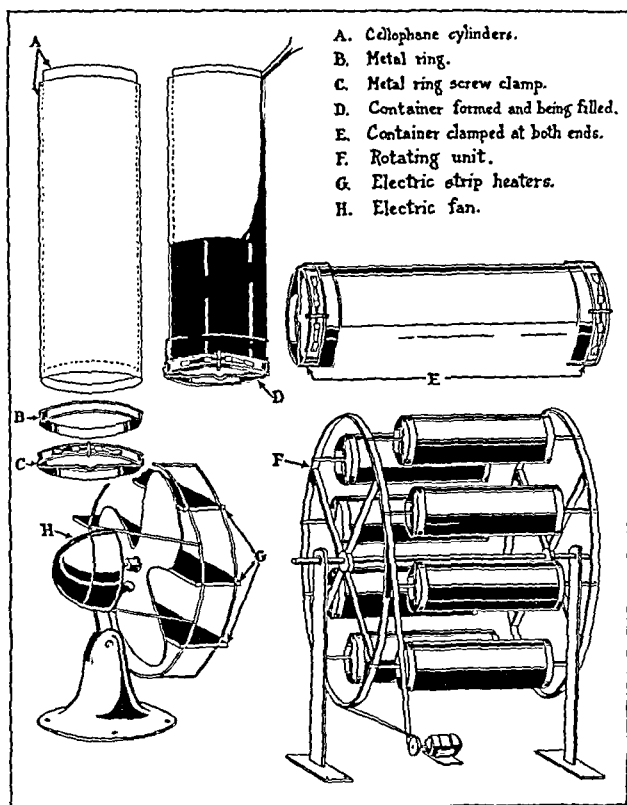
8. Thalheimer, William: A Simple Inexpensive Method for Concentrating Serum Under Sterile Conditions, *Soc. Proc. Exper. Biol. & Med.* 37: 639-641 (Jan.) 1938.

9. Hartman, F. W.: The Elimination of Rubber Tubing on Intravenous Sets, *Ann. Surg.* 111: 495-501 (March) 1940.

preparation of the cylinders they are washed in distilled water and then boiled in two changes of double distilled water for ten minutes. They are then again thoroughly rinsed with double distilled water. Now the sealing ring is applied at one end and double distilled water is run in to test for leaks. With the second sealing ring the cylinders are placed in a large Petri dish and sterilized with steam for twenty minutes at 30 pounds pressure. The cylinders must be kept moist throughout sterilization and until filled with plasma. Filling is done in a small closed room. The cylinders are separated with sterile forceps and the plasma is pipetted or poured between the inner and the outer cylinder. Then the edges are approximated and air filtered through cotton is introduced. The ends of the two cylinders are folded over twice and the sealing ring is put in place. The filled and sealed container is now attached to the rotor by means of heavy rubber bands.

As the rotation takes place the plasma comes in contact with the entire surface of the inner and outer cellophane cylinders, and mixing with the air produces marked foaming, which increases as the concentration of the plasma proceeds. As a result of the rotation and foaming the residue is desiccated as a light, airy froth which breaks up into porous flakes or crystals. The rate of desiccation of plasma ranged from 60 to 75 cc. an hour in the small cylinders (14 by 4½ inches) and from 130 to 160 cc. an hour in the larger cylinders (22 by 6½ inches).

After desiccation the froth is broken into flakes or crystals by gently working the cellophane cylinders between the fingers or hands. The cylinders are then folded and placed in flat tin boxes of appropriate size, sealed with "scotch" tape.



Apparatus used for desiccating blood plasma.

When the desiccated plasma is to be regenerated the cellophane cylinders are cut cleanly across with flame sterilized scissors or knife and the flakes are poured into the proper amount of sterile distilled water. From two to five minutes of shaking suffices to give a good solution which remains stable for a number of days at 4 C. The solution is usually a light amber and slightly opalescent. The solution is clearer after passage through a Mandler or Seitz filter, but this filtration is unnecessary. The regenerated plasma has been administered to a number of patients without reaction.

In case of an emergency in which distilled water is not available, the desiccated plasma may be regenerated by simply immersing the cylinders in water, as the cellophane is impermeable to bacteria and pyrogens. By rotation, sufficient water is taken up so that a satisfactory though concentrated plasma is obtained in a few hours.

Although the preservation of complement, prothrombin and the like is not considered essential in the desiccation of plasma for intravenous use, since these labile substances are lost for the most part during the storage of the whole blood, we are attempting to preserve these in the cellophane cylinder process by freezing the plasma in a thin layer between the two cylinders, from which the moisture is rapidly extracted without vacuum.

Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

INTRODUCTION

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CHICAGO

More than fifteen years have passed since there appeared the first collection of articles on "Glandular Physiology and Therapy," published under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association. Our knowledge has advanced more in these fifteen years than in all the previous centuries of the life of man. So rapid has been the advance that it was necessary to revise the first series in 1927 and the second in 1935. With the passing of the third five-year period, the Council on Pharmacy and Chemistry has considered it desirable again to survey the advancement of our knowledge.

Conspicuous among the reasons for publishing a summary of endocrinology in 1924 was the existence of a pseudoscientific therapy based on glandular materials promoted by pharmaceutical manufacturers with but slight evidence as to actual utility. Much of this empirical and unwarranted therapeutics has disappeared. With the establishment of a new Food and Drug Law and with the coming of the new powers given to the Federal Trade Commission under the Wheeler-Lea Bill, it is likely that still further improvement will occur. The sale of extracts of tonsil, kidney, spleen and heart and, indeed, of mixtures of these with innumerable other preparations, is likely to be better controlled in the future than it has been in the past. No doubt obvious charlatanism will be controlled. However, the difficulty of evaluating therapeutic results and the great psychologic factor involved in most glandular disturbances combine to confuse considerably many physicians who, witnessing the marvels of scientific glandular therapy, are ready to accept as established claims for much that is in no way proved.

The entire volume published in 1927 included only 98 pages. The series issued in 1935 included thirty-one contributions and made a book of 528 pages. In the present series the number of manuscripts is not greatly increased but the amount of material is considerably larger. Particularly important are the articles concerned with the endocrinology of the female reproductive mechanism. Interesting also are those articles which discuss new aspects of our knowledge of the adrenal and the pituitary. Extraordinary advances have been made with reference to the antihormones. Of special importance also are those articles which discuss the interrelationships of various portions of the glandular

apparatus. The investigators who have contributed to this series of articles are all men of note in the fields about which they write.

When the publication of this series of articles in THE JOURNAL is completed, the material will again be made available in book form under the title "Glandular Physiology and Therapy."

RELATIONSHIP OF ANTERIOR LOBE OF THE HYPOPHYSIS TO OTHER ENDOCRINE GLANDS

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NEW YORK

This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—Ed.

The laboratory and clinical research which has been carried on since the last edition (1935) of *Glandular Physiology and Therapy* has not revealed any essentially new interrelationships between the hypophysis and the other glands of internal secretion. Nor have investigations revealed that any of the interrelationships of the hypophysis given in the last edition were erroneous. Important investigations have been reported, however, during this period. Those in the field of carbohydrate and fat metabolism have been especially fruitful. Contributions of preceding years, among which those from the laboratory of Houssay are especially noteworthy, laid the basis for this subsequent extensive work, which has revealed the importance of the interrelationship between the hypophysis and the adrenal cortex in the metabolism of fats and carbohydrates. The results from the work in this field have not yet sufficiently matured to enable one to determine what practical value they will have in clinical medicine, but they contribute greatly to an understanding of the physiology of the hypophysis.

Some advance has been made in the purification of preparations containing the pituitary hormones, though the advances, owing to the protein nature of these hormones, have not kept pace with those made in investigations on the chemically more simple hormones (steroids) of the adrenal gland and the gonads.

Aside from the so-called metabolic principles, five hormones or principles continue to be generally recognized as issuing from the anterior lobe of the hypophysis. These are: (1) the growth (somatotrophic) principle; (2) the gonadotrophic hormone(s) or complex; (3) the thyrotrophic hormone; (4) the corticotrophic (adrenotrophic) hormone, and (5) the lactogenic hormone.¹ The evidence for the secretion of these separate factors is based on data secured from (1) the effects of hypophysectomy and (2) the effects of the injection of hypophysial extracts in (a) animals in which an endocrine deficiency has been established by the ablation of one of the endocrine glands, usually the hypophysis, and (b) normal animals.

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1. Other hormones from the hypophysis have been described, but their existence and action are not as well established as the existence and action of the five listed. These other tropic hormones are a medullotrophic (Collier) and a pancreatotrophic hormone (Anselmino, Harold and Hoffman).

EFFECTS OF HYPOPHYSECTOMY

The syndrome from a total deficiency of the anterior lobe of the hypophysis has been studied in all common laboratory animals, in monkeys and in man (Simmonds's disease). The studies are revealing in regard to the relationship of the hypophysis to the other glands of internal secretion and so merit a brief description.

The picture presented after hypophysectomy is quite uniform throughout all species of animals. The thyroid, the adrenal cortex and the gonads and accessory reproductive organs undergo profound involution, and their functional activity is greatly reduced. Parathyroid changes are less definite. Lactation ceases abruptly. The thymus involutes, although this may be an indirect effect. The capacity for muscular work is decreased, and activity is reduced: The appetite is diminished, hypoglycemia of varying degrees of severity develops, the circulation becomes sluggish, and the blood pressure is lowered. In young animals growth ceases abruptly, although very young rats may grow slightly. The viscera are small. Resistance to trauma and infection is greatly diminished, and the basal metabolism is lowered. The resultant effect, then, is atrophy or involution of most of the endocrine glands and polyglandular deficiency. Survival for extensive periods, however, is possible and is dependent to a considerable extent on maintaining the normal food intake and so preventing hypoglycemic coma or convulsions (especially in rabbits and monkeys) and on maintaining normal body temperature. Less care seems to be necessary with rats, ferrets and dogs in order to secure prolonged survival than with other species, including man. It is not probable that even with the greatest care any animal with complete ablation of the anterior lobe of the hypophysis will survive for a normal life span.

A small fragment of functioning gland is able, however, to maintain an animal in an apparently normal condition, and even a fragment of microscopic size has some effect.² In rats as little as 10 per cent of the gland will prevent the development of the disabilities, and in monkeys certainly not more than one fourth of the gland is necessary. The hypophysis thus has a great margin of safety, as is true for the other endocrine glands. A fragment which remains appears to have little or no capacity to regenerate, although with regard to this data on monkeys and man are not available.

Experimental work has not sufficed to elucidate the condition of hypofunction in a gland of normal size, for such a condition has not been reported to occur in animals and therefore cannot be studied in them. It is essentially a clinical problem, arising in certain cases from a preponderance of nonsecretory (chromophobe) cells at the expense of secretory (chromophil, i. e., acidophil and basophil) cells.

Experimentally it has been found that a genetic deficiency of one of the two secretory cell types of the anterior lobe of the hypophysis may exist. In the particular strain of mice in which this defect appeared, the acidophils were totally absent, but the chromophobes and basophils were present.³ The disabilities of hypophysectomy were all present except the atrophy of the genitals, thus supplying additional significant evidence that the basophils elaborate the gonadotrophic hormone

2. The literature is reviewed by Smith, P. E., in Allen, Edgar; Danforth, C. H., and Doisy, E. A.: *Sex and Internal Secretions*, ed. 2, Baltimore, Williams & Wilkins, 1939, p. 391.

3. Smith, P. E., and MacDowell, E. C.: *The Differential Effect of Hereditary Mouse Dwarfism on the Anterior Pituitary Hormones*, *Anat. Rec.* 50:85 (July 25) 1931.

complex. That a similar condition may occasionally exist in the human subject is indicated in a case recently reported by Shorr and co-workers.⁴ The opposite condition, overactivity of a cell type, has long been known from studies on acromegaly, in which there is a tumor of the acidophils.

Experimental and clinical work on the anterior lobe of the hypophysis thus shows that this gland influences, and in most cases directly controls, all of the other glands of internal secretion. These interrelations were all established at the time that the last edition of this book was published, and much of the work since then has been directed toward determining the number of hormones elaborated by the hypophysis and their action and toward the purification of preparations of these hormones.

ACTION OF PITUITARY HORMONES

The Growth Principle.—That the secretion of the hypophysis is essential for general body growth except in the earlier stages of development is unquestionable. The question of the existence of a specific growth-promoting principle would appear to have been raised largely for three reasons: 1. Preparations of the growth-promoting factor have not been free from substances affecting specific organs—thyroid glands, gonads and adrenal glands. 2. Growth is such a complex process, as has been especially pointed out by Stockard,⁵ that it is difficult to conceive of its being due to a single hormone. Each of the pituitary tropic hormones is essential for the growth of the specific organ which it affects. 3. The injection of prolactin—a lactogenic factor—causes growth in pigeons and dwarf mice, as shown by Riddle and collaborators.⁶ Moreover, in still lower forms (amphibian larvae) the hypophysis can be ablated without inhibiting growth to any great extent.

Specific endocrine stimuli, however, seem to be more necessary for the promotion of growth in mammals than in lower forms, and an interest in comparative physiology should not blind one to the fact that in medical practice the responses of mammals, especially those of man, are of predominant interest. In regard to the contamination of extracts of the growth factor with other anterior pituitary factors, it has been greatly reduced without impairing the growth-stimulating property of the extract.⁷ It thus appears, as stated by Evans nearly twenty years ago, that in mammals a specific principle is secreted by the hypophysis which is essential for general body growth. This principle appears to influence skeletal growth mainly by stimulating the epiphyseal cartilages, although the effect extends to the soft tissues and the viscera, also.

The Gonadotropic Complex.—The investigations reported by Cushing and collaborators and by Aschner on dogs some thirty years ago revealed that the gonads atrophied after hypophysectomy. Work in 1927 in which atrophic gonads of hypophysectomized rats were repaired and immature ovaries were stimulated to precocious development by administration of pituitary

extract gave conclusive proof that there was a factor (or factors) secreted by the hypophysis which was necessary for the structural and functional maintenance of the gonads and through them of the accessory reproductive organs. It was soon discovered, however, that the injection of extracts of hypophyses from different species did not give equal quantitative responses of the different types of tissue composing the gonads. In fact, Evans and Long showed in 1922 that crude extracts of beef hypophyses caused the formation of large amounts of lutein tissue in the ovaries of normal mature rats but had no follicle-stimulating effect. When it was found that the hypophyses of other species—rats, horses, sheep, man—gave pronounced follicle-stimulating effects, indirect evidence was thus supplied that more than one gonadotropic hormone had been encountered.

Fractionation and purification of gonadotropic extracts were undertaken by several investigators (Fevold, Hisaw and Leonard,⁸ Wallen-Lawrence,⁹ Evans and associates¹⁰). The present consensus from the laboratories in which these studies are being made is that two gonadotropic principles are elaborated by the anterior lobe of the hypophysis. The determination of the number of gonadotropic hormones is not easy to make, however, and in my opinion has not been definitely made. The length of treatment, the rate of absorption, the dosage and the site of injection (subcutaneous or intraperitoneal) all influence the response. That the solution of the problem is difficult is attested by the fact that within a six year period investigators in one prominent laboratory have stated that there was only one, that there were four and later that there were two pituitary gonadotropic hormones. The two postulated hormones are usually designated as the follicle-stimulating and the luteinizing hormone. The second hormone is sometimes designated as the interstitial cell-stimulating hormone instead of the luteinizer.

The hypophysial luteinizing hormone is not identical with the gonadotropic principle of human pregnancy urine, which is sometimes designated as the luteinizing hormone.¹¹ Little is known of the chemical composition of the gonadotropic factors, a statement which is also true of the other hypophysial principles.

The Thyrotropic Hormone.—It has been known since the classic work of Rogowitsch in 1889 that the hypophysis is influenced by the thyroid. The determination of an effect of the hypophysis on the thyroid is much more recent. This effect was first demonstrated by hypophysectomy and the injection of hypophysial extracts in amphibia¹² and later in mammals.¹³ The

4. Reported at the Annual Meeting of the Association for the Study of Internal Secretions in June 1940.

5. Stockard, C. R. in discussion on Evans.

6. Aspect Am. J. phil. Growt. Nerv. Fraen Prepa Thyrotropic hormones, L. and Schooley, J. P.: the Action of Prolactin, tes, R. W.; Laanes, Theodor, Me. Free from Lactogenic and 7) 1939.

8. Fevold, H. L.; Hisaw, F. L., and Leonard, S. L.: The Gonad-Stimulating and Luteinizing Hormones of the Anterior Lobe of the Hypophysis, Am. J. Physiol. 97: 291 (May) 1931. Fevold, H. L.: The Follicle-Stimulating and Luteinizing Hormones of the Anterior Pituitary, in Allen, Edgar; Danforth, C. H., and Doisy, E. A.: Sex and Internal Secretions, Baltimore, Williams & Wilkins Company, 1939, p. 966.

9. Wallen-Lawrence, Zonja: Proof of the Existence of a Follicle-Stimulating and a Luteinizing Hormone in the Anterior Lobe of the Pituitary Body, J. Pharmacol. & Exper. Therap. 51: 263 (July) 1934.

10. Evans, H. M.; Korpi, Karl; Simpson, Miriam E.; Pencharz, R. J., and Wonder, D. H.: On the Separation of the Interstitial Cell Stimulating, Luteinizing and Follicle Stimulating Fraction in the Anterior Pituitary Gonadotropic Complex, Univ. California Publ. Anat. 1: 255, 1936.

11. Some commercial descriptive advertisements are misleading in that it is indicated that the hormones from these two sources are identical. All the evidence indicates that the gonadotropic substance in human pregnancy urine is from chorionic tissue, not the hypophysis.

12. The literature is reviewed by P. E. Smith (Relations of the Activity of the Pituitary and Thyroid Glands, in Harvey Lectures, Baltimore, Williams & Wilkins Company, 1930, p. 129).

13. Loeb, L., and Bassett, R. B.: Effect of Hormones of Anterior Pituitary on Thyroid Gland in the Guinea-Pig, Proc. Soc. Exper. Biol. & Med. 26: 860 (June) 1929. Aron, M.: L'hormone préhypophysaire excito-sécrétrice de la thyroïde, Rev. franç. d'endocrinol. 8: 472 (Dec.) 1930.

threshold of the stimulus of structural response differs greatly in different species, the thyroids of rats being unchanged in structure by high doses of pituitary thyrotropic extract, whereas the thyroids of guinea pigs and rabbits undergo profound changes even with low doses. The injection of the thyrotropic extract in responsive species results in most of the thyroid changes characteristic of exophthalmic goiter, i. e., increase in size of the thyroid, depletion of iodine, loss of colloid, and hyperplasia and hypertrophy of the cells, with the characteristic irregular type of follicles. The infiltration by lymphocytes and the increase in connective tissue characteristically present in hyperplasia of human thyroids are not present in the hyperplasia experimentally induced. The absence of these changes may be due to the shortness of the period of treatment.

The injection of thyrotropic extract causes also a rapid and marked rise in basal metabolism, although a rise in metabolic rate from pituitary extract has also been reported in thyroidectomized animals.¹⁴ The thyrotropic extract induces a hyperplastic response of thyroid tissue *in vitro*¹⁵ and also of transplanted thyroids;¹⁶ so it can act independently of any innervation. In man massive doses have been shown to be effective in cases in which hypothyroidism is due to underfunction of the pituitary and not to lack of responsiveness of the thyroid. The thyrotropic extract of pituitary may have a limited field of usefulness, in that its administration will give information as to whether or not hypothyroid states are due to lack of responsiveness of the thyroid to stimulation by the hypophysis. It seems improbable, however, that it can have any extensive clinical usefulness.

The Corticotropic Hormone.—A stimulating action of the anterior lobe of the hypophysis on the adrenal cortex was first shown in amphibia. Hypophysectomy caused profound atrophy of the cortical but not of the medullary component of the adrenal, an action which was confirmed in mammals some ten years later.¹⁷ The atrophy could be prevented or the involuted glands restored to a normal condition by the administration of anterior lobe. There has been much question as to whether or not this cortex-stimulating action of the hypophysis was due to a distinct hormone, but the evidence supplied by Collip and co-workers,¹⁸ Moon¹⁹ and others shows that it is distinct from the thyrotropic, growth-promoting lactogenic and other hypophysial hormones. It appears to have no action other than that of stimulating the cortex of the adrenal.

14. This effect is stated to be due to a specific metabolic principle and not to a tropic hormone (Collip). This principle is remarkably thermostable and is resistant to boiling in dilute acid and alkali and to peptic digestion. Its injection causes a sharp rise in the metabolic rate for only a few hours. Collip states that it probably has its origin in the pars intermedia but that it is not identical with the melanophore-expanding hormone.

15. Eitel, Hermann; Krebs, H. A., and Loeser, Arnold: Hypophysen-15: Die Wirkung der thyreotropen Substanz auf die Schilddrüse *in vitro*, Klin. Wchnschr., 33.

16. Houssay, B. A.; Biasotti, A., and Magdalena, A.: Hipófisis y tiroides: Acción del extracto del lóbulo anterior de la hipófisis sobre la histología de la tiroidea del perro, Rev. Soc. argent. de biol. 8:130 (May-June) 1932. Marine, David, and Rosen, S. H.: The Effect of the Thyrotropic Hormone on Auto- and Homotransplants of the Thyroid and Its Bearing on the Question of Secretory Nerves, Am. J. Physiol. 107: 677 (March) 1934.

17. Smith, P. E.: The Pigmentary, Growth and Endocrine Disturbances Induced in the Anuran Tadpole by the Early Ablation of the Pars Buccalis of the Hypophysis, in American Anatomical Memoirs, Philadelphia, Wistar Institute of Anatomy and Biology, 1920, No. 11; Hypophysectomy and a Replacement Therapy in the Rat, Am. J. Anat. 45: 205 (March) 1930.

18. Collip, J. B.; Anderson, E. M., and Thomson, D. L.: Adrenocortical Hormone of Anterior Pituitary Lobe, Lancet 2: 347 (Aug. 12) 1933.

19. Moon, H. D.: Preparation and Biological Assay of Adrenocorticotrophic Hormone, Proc. Soc. Exper. Biol. & Med. 35: 649 (Jan.) 1937.

The injection of a pituitary extract containing the corticotropic factor restores the adrenals after hypophysectomy. It partly restores the work capacity of hypophysectomized animals, although their work capacity still remains somewhat subnormal, as is the case also when cortical extracts are administered.²⁰

The injection of cortical extract has been shown to repress the liberation of corticotropic hormone from the hypophysis.²¹ It seems probable that the enlargement of the adrenals in normal animals under conditions of stress is due to liberation of unusual amounts of corticotropic hormone by the hypophysis.

As in the case of the thyrotropic extract, it is not probable that the corticotropic extract will prove of much clinical value.

The Lactogenic Hormone.—The pituitary lactogenic hormone (prolactin; galactin; mammatropin) is purely a secretagogue and does not cause development and growth of the mammary glands. It is the only pituitary hormone that has been secured in crystalline form,²² although the potency of the crystals does not exceed and even may not equal that of the amorphous powder.

The test used for determining lactogenic activity is the response of the crop gland of the pigeon. Riddle has shown that his special preparation, prolactin, has other effects in pigeons, stimulating general body growth and the gastrointestinal tract. These effects are not secured in mammals by the injection of prolactin. Prolactin also stimulates the basal metabolic rate of thyroidectomized pigeons.²³

The injection of prolactin gives but a temporary increase in milk production in cows,²⁴ and clinical studies show little or no response following its injection in man.²⁵

Relations of the Anterior Lobe of the Hypophysis to Carbohydrate and Fat Metabolism.—The interrelationships of the anterior lobe of the hypophysis and other internal secretory glands in carbohydrate and fat metabolism is a subject which is complex. The reported studies dealing with the injection of pituitary extracts concern themselves largely with "effects" produced by very crude extracts, for the principle or principles producing these effects are in most cases very labile and a degree of purification equal to that achieved with the other pituitary factors has not been obtained. These studies, particularly those of Long and Lukens, have shown an important interrelationship between the hypophysis and the adrenal cortex in carbohydrate metabolism.

Although this complex interrelationship will be discussed more fully in another section, it seems justifiable to discuss briefly some phases of it here. Certain important findings stand out in this work. These are: (1) the greatly increased sensitivity to insulin of hypophysectomized animals, first reported by Houssay and Magenta, in 1924, which was shown later to be due

20. Ingle, D. J.; Moon, H. D., and Evans, H. M.: Work Performance of Hypophysectomized Rats Treated with Anterior Pituitary Extracts, Am. J. Physiol. 123: 620 (Sept.) 1938.

21. Ingle, D. J.: The Effects of Administering Large Amounts of Cortin on the Adrenal Cortices of Normal and Hypophysectomized Rats, Am. J. Physiol. 124: 369 (Nov.) 1938.

22. White, Abraham; Catchpole, H. R., and Long, C. N. H.: Crystalline Protein with High Lactogenic Activity, Science 86: 82 (July 23) 1937. Shipley, R. A.; Stern, K. G., and White, Abraham: Electrophoresis of Anterior Pituitary Proteins, J. Exper. Med. 69: 785 (June) 1939.

23. Riddle, Oscar; Smith, G. C.; Bates, R. W.; Moran, C. S., and Lahr, E. L.: Action of Anterior Pituitary Hormones on Basal Metabolism of Normal and Hypophysectomized Pigeons and on the Paradoxical Influence of Temperature, Endocrinology 20: 1 (Jan.) 1936.

24. Folley, S. J., and Young, F. G.: The Effect of Continued Treatment with Anterior Pituitary Extracts on Milk Volume and Milk-Fat Production in the Lactating Cow, Biochem. J. 23: 192 (Feb.) 1939.

25. Stewart, H. L., and Pratt, J. B.: Effect of Prolactin on Mammary Gland Secretion, Endocrinology 25: 347 (Sept.) 1939.

to the loss of the anterior lobe only (Houssay and Potick²⁶); (2) the amelioration of experimentally induced diabetes by hypophysectomy, reported by Houssay and Biasotti²⁷ in 1930 and frequently referred to as "the Houssay phenomenon"; (3) the production of temporary diabetes by injection of anterior pituitary extracts²⁸ and the production of permanent diabetes by a relatively short course of injections of increasing doses of crude pituitary extracts prepared at low temperatures, reported by Young²⁹ (diabetogenic effect), in which there is an injury of the islands of Langerhans in the pancreas,³⁰ with reduction of the pancreatic content of insulin;³¹ (4) the amelioration by adrenalectomy of diabetes induced by pancreatectomy, reported by Long and Lukens,³² and (5) the reinstitution of the diabetic condition by the injection of massive doses of extract of adrenal cortex, reported by Lukens and Dohan.³³ The injection of pituitary extracts causes ketosis in fasting animals.³⁴ It also will inhibit the action of injected insulin (glycotropic action of Young³⁵) and will maintain the levels of muscle glycogen in fasting hypophysectomized animals (glyco-static effect³⁰). The rate of absorption of carbohydrates by the intestine, which is decreased by hypophysectomy, can be restored to normal by the administration of thyroid.³⁷

It is tempting to ascribe these various metabolic effects to separate hormones but, as emphasized by Long,³⁸ this is not justifiable with the evidence available.

For the maintenance of diabetes after pancreatectomy, the presence of the adrenal glands has been shown to be essential by Long and Lukens. The ablation of these glands ameliorates the diabetic condition, and although amounts of cortical extract sufficient to maintain the life and health of the experimental animal do not restore the diabetic condition, massive doses will cause recurrence.³⁹ It appears that the pituitary stimulation of the adrenals, mediated by the corticotrophic hormone, is thus essential for the maintenance of the diabetic condition in experimental animals. The opposite condition, hypo-

glycemia, characteristic of fasting hypophysectomized animals, appears to be attributable, at least in part, to the absence of the stimulating effect of the hypophysis on the adrenals.

Ketosis from the injection of pituitary extract is also dependent on the presence of the adrenals, for this condition is diminished by adrenalectomy.³⁸ The inhibiting effect of injected pituitary extract on injected insulin (glycotropic action) and the maintenance of muscle glycogen in fasting hypophysectomized animals by the injection of pituitary extract appear to be direct effects, not involving the adrenals.³⁸

The inactivation of the thyroid induced by hypophysectomy apparently explains the decreased rate of carbohydrate absorption of pituitaryless animals. Althausen⁴⁰ showed that the injection of thyroxine increases the rate of absorption of sugars by the intestine in normal rats, and Russell,³⁷ following this lead, was able to show that thyroxine restored the normal rate of carbohydrate absorption in hypophysectomized rats. The dose necessary was less than that required for the restoration of the metabolic rate. It thus seems justified to refer the decrease in the rate of absorption of sugars after hypophysectomy to the loss of the thyrotrophic hormone and the consequent inactivation of the thyroid.

The observations made in experimental work on the role of the anterior lobe of the pituitary and the inter-relationship to other internal secretory glands in carbohydrate and fat metabolism, although of potential importance in medical practice, are not for the most part clinically applicable at present. An exception can perhaps be made with regard to the results of this work relating to the genesis of diabetes mellitus. Although it is generally recognized that many persons with diabetes do not show the islet lesions and thus differ from dogs made permanently diabetic by the injection of pituitary extracts, nevertheless, in other diabetic persons such lesions are present, and it seems not unreasonable to believe that overactivity of the hypophysis was a factor in causing this injury of the islets. As shown by White⁴¹ and others, the incidence of diabetes is higher in children who are unusually tall for their age than it is in those whose growth has not been so rapid, an observation which suggests that increased activity of the hypophysis may be associated with the juvenile onset of this disease. It is also reasonable to assume that there are variations in the susceptibility of the pancreatic islets of different persons to injury. Permanent diabetes does not develop in all dogs from the injection of diabetogenic pituitary extract, and in other species (rats, cats) no injury to the islets results from the injection of such a pituitary extract unless part of the pancreas has been removed.

RECIPROCAL ACTION OF INTERNAL SECRETIONS ON THE HYPOPHYSIS

The functional activity of the hypophysis, i. e., the rate of formation and release of the various pituitary hormones, is influenced by the secretion of the other endocrine glands, so that a balance exists between the various glands. This balance is also influenced by the activity of the other tissues and organs of the body and provides a mechanism which is responsive to the needs of the body. Some examples of the response of

26. Houssay, B. A., and Potick, D.: Antagonisme entre l'hypophyse et l'insuline chez le crapaud, *Compt. rend. Soc. de biol.* **101**: 940 (July 17) 1929.

27. Houssay, B. A., and Biasotti, A.: Le diabète pancréatique des chiens hypophysectomisés, *Compt. rend. Soc. de biol.* **105**: 121 (Oct. 16) 1930.

28. Evans, H. M.; Meye, F. L.; Simpson, Miriam E., and Reichert, F. L.: Disturbances of in Normal Dogs Injected with the Hypophysis, *Soc. Exper. Biol. & Med.* **25**: 857 (April) 1930. Glycosuria in Rabbits Followed by Pituitary, *ibid.* **29**: 1220 (June) 1932.

29. Young, F. G.: Permanent Experimental Diabetes Produced by Pituitary (Anterior Lobe) Injections, *Lancet* **2**: 372 (Aug. 14) 1937.

30. Richardson, K. C., and Young, F. G.: Histology of Diabetes Induced in Dogs by Injection of Anterior-Pituitary Extracts, *Lancet* **1**: 1098 (May 14) 1938.

31. Campbell, James, and Best, C. H.: Production of Diabetes in Dogs by Anterior-Pituitary Extracts, *Lancet* **1**: 1444 (June 25) 1938.

32. Long, C. N. H., and Lukens, F. D. W.: Effects of Adrenalectomy and Hypophysectomy upon Experimental Diabetes in Cat., *J. Exper. Med.* **63**: 465 (April) 1936.

33. Lukens, F. D. W., and Dohan, F. C.: Further Observations on the Relation of the Adrenal Cortex to Experimental Diabetes, *Endocrinology* **22**: 51 (Jan.) 1938.

34. Burn, J. H., and Ling, H. W.: Excretion of Acetone Bodies on Fat Diet as Affected by Injection of Pituitary (Anterior Lobe) Extract and by Pregnancy, *Quart. J. Pharm. & Pharmacol.* **6**: 31 (Jan.-March) 1933.

35. Young, F. G.: The Identity and Mechanism of Action of the Glycotropic (Anti-Insulin) Substance of the Anterior Pituitary Gland, *Biochem. J.* **32**: 1521 (Sept.) 1938.

36. Bennett, L. L.: The Interrelation of Pituitary and Adrenal in the Control of Carbohydrate Levels in the Rat, *Endocrinology* **22**: 193 (Feb.) 1938.

37. Russell, J. A.: The Effect of Thyroxine on the Carbohydrate Metabolism of Hypophysectomized Rats, *Am. J. Physiol.* **122**: 547 (June) 1938.

38. Long, C. N. H.: Diabetes Mellitus in the Light of Our Present Knowledge of Metabolism, *Tr. & Stud., Coll. Physicians, Philadelphia* **4**: 21 (April) 1939.

39. Lukens, F. D. W., and Dohan, F. C.: Further Observations on the Relation of the Adrenal Cortex to Experimental Diabetes, *Endocrinology* **22**: 51 (Jan.) 1938.

40. Althausen, T. L.: Influence of the Thyroid Gland on Intestinal Absorption of Dextrose, Galactose, and Xylose, *J. Clin. Investigation* **16**: 658 (July) 1937.

41. White, P.: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932.

the endocrine glands to environmental conditions are the hypertrophy of the adrenal cortex under conditions of stress (cold, toxins, and so on), the hyperplasia of the thyroid of the animal kept in a cold environment, and the enlargement and activation of the gonads in some birds and some mammals, which have a seasonal breeding period, with increased light.⁴² Some of the responses, at least, are due to increased activity of the hypophysis. Activation and enlargement of the gonads can be induced in the winter season and in some immature animals by increased illumination. After removal of the eyes, gonad activation can be induced in some birds by direct illumination of the hypophysis through a tube leading to that gland.⁴³

Adrenal and Hypophysis.—In a series of papers Ingle²¹ has shown that the injection of an extract of adrenal cortex causes a regression of the adrenal cortex which is nearly equal to that resulting from hypophysectomy and that this regression is due to a decrease in the output of corticotrophic hormone by the pituitary, for the injection of a corticotrophic extract of the pituitary prevented the cortical atrophy. It has been mentioned that the adrenal cortex atrophies after hypophysectomy. In intact animals the cortex hypertrophies under conditions of stress, but in hypophysectomized animals this hypertrophy does not take place. If placed in the cold, the animals thus operated on will succumb at temperatures which will be survived by normal animals or by hypophysectomized animals given an extract of adrenal cortex. Although it cannot be assumed that the adrenal glands are alone responsible for survival with noxious stimuli or under conditions of increased stress, nevertheless they are an important factor in the resistance and survival. The immediate stimulus causing the hypertrophy is the corticotrophic secretion of the hypophysis.

Gonads and Hypophysis.—The mechanism operating between the gonads and the hypophysis is similar to that described for the adrenals and the hypophysis. Both clinical and experimental studies show this interrelationship. The fact that the pituitary gonadotropic substance is excreted in man in the urine has given an unexcelled opportunity to study the factors which influence its secretion. The output of gonadotropin in the urine increases in amount if the gonads are removed or undergo involution, as at the menopause. As has been extensively shown by clinical studies, the administration of gonadal products, especially the estrogens, represses this enhanced output. In experimental animals the removal of the gonads results in increased potency of the pituitary, with an increase in the number of basophils. These structural changes can be prevented or the normal structure restored by the injection of estrogen or androgen.

Thyroid and Hypophysis.—Although a structural alteration of the hypophysis from the extirpation of an endocrine gland was first noted from thyroidectomy, and the administration of thyroid alters the proportion and structure of certain of the cell types of the hypophysis, nevertheless a demonstration of the influence of thyroxine on the functional activity of the hypophysis as complete as that in the case of the gonads and adrenals has not been given. The evidence, however, indicates that the output of thyrotrophic hormone

is repressed by unusual amounts of thyroid secretion. The administration of thyroid causes an involution of this gland, an effect which by analogy with relationships already discussed is presumably due to a decreased output of thyrotrophic hormone. Attempts to assay the urinary excretion of the thyrotrophic substance have given conflicting results.

In the preceding discussion it has been shown that excessive amounts of the secretion of the gonads, of the cortex of the adrenal and probably also of the thyroid inhibit the corresponding tropic hormones of the hypophysis, thus supplying an important mechanism for the maintenance of a balance between the hypophysis and each of these glands. There is also some evidence that an excessive amount of secretion of one of these glands influences the rate of secretion of the pituitary tropic hormones affecting other glands or structures. The administration of excessive amounts of estrogen promptly inhibits the growth of experimental animals and will inhibit the development of the mammary glands. The administration of thyroid increases the gonadotropic potency of the hypophysis, although the opposite condition, thyroid deficiency, does not reduce the pituitary content of gonad-stimulating hormone. The inhibiting effect of thyroidectomy on growth can be prevented by administering a hypophysial extract containing the growth-promoting factor, so that the inhibition probably is due, in part, to decreased secretion of this growth hormone.

RESPONSIVITY OF ENDOCRINE ORGANS AND OTHER TISSUES TO ENDOCRINE PRODUCTS

It is a fundamental tenet of the concept of internal secretion that the endocrine organs secrete chemical hormones ("messengers") which have specific effects, whether their action is on other endocrine organs, on a tissue group or on all the tissues of the body. This concept, however, does not justify the assumption that a hormone will induce its characteristic effect in all cases. In other words, a capacity of the end organ to respond to a hormone is also essential. Of the many examples which show this, two only will be given. Growth depends not only on the presence of the growth factor but on the responsivity of tissue, as is well shown by results obtained from injections of an extract containing the growth-promoting factor in two races of dogs—dachshund and collie. The injections in the former stimulate primarily a growth in the length of the vertebral column; the injections in the latter, an increase in the length of the legs.⁴⁴ There seems to be an inherent, hereditary capacity of response in the vertebral and appendicular components of the skeleton, respectively, in these two strains of dogs. The importance of the growth responsivity of various structures of the body has also been shown by breeding experiments in dogs. Experimental work on the gonads shows that at early ages some of the components of these glands are unresponsive to gonadotropic hormones; responsivity develops with aging. Although the gonadotropic hormones are essential to sexual maturation, it would not be justifiable to attribute sexual maturity solely to the onset of the secretion of these hormones; the development of responsivity to these hormones is also an essential factor. The responsivity of the end organ thus plays an important part in the action and the interrelations of the endocrine glands.

42. The extensive literature is reviewed by M. A. Bissonnette (The Influence of Light upon Pituitary Activity, A. Research Nerv. & Ment. Dis., Proc. [1936] 17: 361, 1938).

43. Benoit, J.: Etude du mécanisme de la stimulation par la lumière de l'activité testiculaire chez le canard domestique, Bull. biol. 71: 393, 1937.

44. Evans, H. M.; Meyer, Karl, and Simpson, Miriam E.: The Growth and Gonad-Stimulating Hormones of the Anterior Hypophysis, Memoirs of the University of California, Berkeley, Calif., University of California Press, 1933, vol. 11.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION
OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

DANGERS INCIDENT TO THE INDISCRIMINATE USE OF RADIUM COMPOUNDS OR RADON

IN THE TREATMENT OF CUTANEOUS DISEASES

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Radium from abroad has found anxious and eager buyers in this country during the past decade. Nine tenths of the radium mined each year finds a use in medicine.¹ The United States is probably the largest consumer of radium and radon for medical purposes, and the decreased cost resulting from a greater supply has made them available for wider distribution.

Formerly American dermatologists received but little instruction in the physical and chemical properties and the uses of radium. With each successive year there has been increased knowledge of the clinical applications of radium and radon. The modern dermatologist utilizes radioactive elements more efficiently than his predecessors and with discriminating judgment.

Notwithstanding increased knowledge, it is regrettable that some physicians, including dermatologists, use radium or radon for the treatment of various dermatoses without having had adequate training of either the disease under treatment or the agent. Some have the fallacious idea that the details of treatment of a lesion requiring irradiation can be obtained from a physicist. Proper treatment of a lesion, no matter how trivial, with an agent so potent as radium or radon requires exact diagnosis and judgment for the selection of the correct dose and technic applicable to the disease. This, of course, means specialized training and knowledge of general dermatology and of that specialized phase of radiology which pertains to dermatology.

The indiscriminate use of radium or radon by an unqualified physician is to be condemned. However, the responsibility also rests with those who sell or rent radium or radon, especially if the medical and physical experts of the distributors give diagnostic aid and suggest treatment without seeing the patient. It is the practice of a few physicians to make a snap diagnosis of a lesion without microscopic confirmation and then seek advice from the radium distributor regarding the dosage, filtration and other technical details. The advice is often given by a physicist or a company physician by mail or over the telephone. Obviously such practice leads to many undesirable results and needless suffering. Because the proper administration of radium treatments requires specialized knowledge, such treatments should be given only by experts who possess complete knowledge of the disease and also of the chemical and physical properties of the therapeutic agent, including dosage measurements. Henry K. Taylor,² chairman of the Special Committee on Radiology of the Medical Society of the County of New York, recently stated: "The

attention of the committee was called to two radium concerns selling their product by mail with instructions for use. The instructions accompanying the radium were issued by doctors who did not have the privilege of examining the patient. This practice is considered unethical." Other physicians and radiologists have had similar experiences.

It is alleged by some that the curtailment of the widespread distribution and use of radium or radon may deny to some the use of this valuable agent. In my opinion this allegation is not true when it is considered that radium or radon when improperly used can cause damage to the tissues and to the patient that may prove to be far more serious than the original condition. In fact, overtreatment with radium or radon can lead to cancer formation. There are many cases of lupus erythematosus, lupus vulgaris, verruca vulgaris, basal cell epithelioma, naevus vasculosus (port wine marks), psoriasis and sycosis vulgaris in which squamous cell epithelioma developed in active lesions of these diseases or in scars following the involution of these lesions as a result of overtreatment with or indiscriminate use of radium or radon. Therefore, unless radiation is properly used in diseases in which this agent is indicated, it is better not to use it. The mere availability of radium or radon does not compensate for the disastrous results following improper use.

Radium and radon should not be rented or sold to persons who are not qualified to use them, because this practice encourages diagnosis and treatment by mail or telephone by an individual who possesses radium or by a corporation engaged in the sale and rental of radium. There is no way that I know of to stop this practice. However, the dangers following the indiscriminate use of radium or radon can be brought to the attention of the practicing physician. Some steps should be taken toward ending the practice of distributors of radioactive substances giving technical information through a salaried physician or physicist who never sees the patient.

The Council on Physical Therapy desires to acquaint all physicians with the undesirable effects observed when radium and radon are used indiscriminately. This article deals only with the dangers resulting from the improper use of radioactive agents in treating diseases of the skin. The errors usually result from incorrect technic, poor judgment or ignorance.

The dermatologist of today is not the externist he was twenty years ago. He knows much more about the causation and management of many dermatoses. The training in the fundamentals of general medicine and in dermatology in particular is much superior to what it was formerly. Eczema, for example, is divided into several varieties. Identification of the particular variety gives clues as to the cause, proper investigation and therapy. In the case of eczema as in other diseases, irradiation with x-rays or radium was used to relieve symptoms and as a cloak to hide inexact diagnosis, lack of therapeutic resourcefulness, ability and knowledge. Now radiation therapy is used less often because of increased knowledge of the dermatoses. In fact, proper topical therapy, hospitalization, controlled environment and so on will usually produce quicker relief than will x-ray or radium therapy.

The improper treatment of certain diseases with radium, radon or x-rays often leads to irreparable damage to the tissues irradiated. Some of these diseases will be discussed.

Dr. George M. MacKee assisted in the preparation of this paper and gave many valuable suggestions.

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1. Importation of Radium, editorial, J. A. M. A. 112: 2069 (May 20) 1939.

2. Taylor, Henry K.: Problems of the Special Committee on Radiology, New York M. Week 19: 4 (July 13) 1940.

CUTANEOUS NEOPLASMS

The physician who treats cutaneous malignant growths should be able to use expertly all the recognized methods of therapy. He should not depend on surgery or irradiation alone. He should be able to use with equal expertness scalpel surgery, electrosurgery, x-rays, radium and radon. The best method or combination of methods should be used for the presenting lesion. The dose of radon, radium or x-rays, the filtration, the distance, the overlapping, the time and other elements should be expertly judged in relation to the size and depth of the lesion, the location, the sex, age and physical condition of the patient and the degree of malignancy. The use of poor judgment in the selection of the proper method of treatment leads to bad results, complications and even death. At this point, I would like to cite an actual case that came to my attention several years ago. An elderly man was treated for a small epithelioma involving the ear with medium voltage and moderately filtered x-rays. It did not respond to the treatment administered and further treatment with x-rays was given. Only a portion of the lesion healed. The remainder was treated with radium. Several months later the lesion had spread and the cartilage and periosteum had been damaged. In addition there were evidences of an acute radiodermatitis. The resistance of the tissues was so lowered that there was also a superimposed eczematous process. Because of this secondary inflammation of the skin, it was impossible to ascertain easily what was dermatitis and what was epithelioma. The pain was so intense that narcotics had to be used for its relief. After the application of soothing remedies, the inflammation subsided. The epithelioma had spread all over the ear, including the external auditory canal and the underlying cartilaginous and bony structures. Extensive surgery was required to ameliorate the condition and reduce the pain. Several years of suffering and convalescence would have been avoided if this patient had been seen by a physician acquainted with all therapeutic methods for such lesions. He would have used a local anesthetic and would have destroyed the entire lesion with electrosurgery or scalpel surgery with plastic repair if necessary. Many other examples of poor results following the improper treatment of cutaneous malignant growths can be cited, but this one case suffices to illustrate the importance of selecting the correct method or combination of methods for the treatment of cancer of the skin.

NEVI

The cavernous and superficial (strawberry) angiomas occurring in children under 1 year of age usually respond well to irradiation. Treatment that may leave x-ray or radium sequelae is contraindicated because many of these lesions may disappear spontaneously. Port wine marks do not respond to irradiation. In fact, many cases which have been treated in the past with radium or radon now show varying degrees of radiodermatitis. No technic now known is safe for the treatment of these lesions. Hairy and nonhairy moles and lymphangiomas respond poorly when treated with radium, radon or x-rays. In fact, any degree of improvement of these lesions is accompanied by a corresponding degree of radiodermatitis.

HYPERTRICHOSIS, HYPERHIDROSIS AND SEBORRHEA

Hundreds of cases of radiodermatitis have been caused by treating hypertrichosis with x-rays and radium. Only a few years ago many beauty parlors were administering x-rays for the treatment of unwanted

hairs on any part of the body. In fact, "chain stores" were established throughout the country to administer the so-called Tricho treatment. Many cases of radiodermatitis resulted from the administration of x-rays by untrained lay operators. Fortunately the "Tricho Institute" no longer exists and American women are now sufficiently educated to avoid x-rays or radium for the treatment of superfluous hair. Irradiation is contraindicated for the treatment of this condition regardless of the technic employed and who employs it. Up to the present writing there is no safe radium or x-ray technic for the permanent removal of unwanted hair. Hyperhidrosis and seborrhea may be benefited by irradiation. No more than a safe amount should be given even though there is failure to cure completely. Much harm results in attempting to cure stubborn cases with x-rays or radium when they fail to respond to a safe dose. Attempting to inhibit permanently all secretory activity of the sweat and sebaceous apparatus with radioactive agents may lead to permanent and harmful changes in the surrounding cutaneous structures.

MYCOSIS FUNGOIDES

Mycosis fungoides, a serious disease of the hemopoietic system which often ends fatally, responds exceedingly well to irradiation. As a rule small doses of x-rays or radium administered at weekly intervals to the affected areas causes the lesions to respond. However, when overtreated there may result serious sequelae affecting the skin as well as the blood forming apparatus. Judicious use of the radioactive agents may keep patients with mycosis fungoides free from lesions for many years and may prolong life indefinitely. In fact, many patients with mycosis fungoides die of other diseases. The fungating and ulcerative stage of this disease is seen infrequently now. This is due to the fact that irradiation with x-rays, radium or radon often controls the disease. In the light of our present knowledge it is a mistake to irradiate the bones, spleen and gland bearing areas with large doses of heavily filtered and high voltage x-rays. The disease affects the skin. Radiation applied directly to the affected skin areas in small doses and whenever indicated is all that is required to cause involution of the presenting lesions and to prevent the formation of the fungating and ulcerative lesions.

KELOIDS

Keloids and other benign new growths and hypertrophies and inflammatory dermatoses such as psoriasis or eczema should not be treated with an amount of radiation sufficient to produce erythema, because even one occurrence of a mild erythema may eventuate in disfiguring and even serious sequelae. Failure to cure a benign condition is not so serious as the harmful results which follow the injudicious use of radiation. Keloids are often only of cosmetic importance. Many lesions are radioresistant, especially the older ones. Therefore forcing the issue with x-rays or radium should be avoided. Overdosage may not only fail to improve the condition but may also lead to irreparable skin damage and even to a neoplasm.

Many other diseases might be discussed in detail, but a sufficient number have been mentioned to demonstrate that overtreatment of dermatologic conditions with radiation leads to disastrous consequences.

Radiation therapy is used with more discrimination by the well trained modern dermatologist. The physician who is not a dermatologist is apt to use radium or x-rays when there are better methods. He is apt

to administer a dose which is too large or he may give too many treatments or the intervals between treatments may be too short. In the presence of congestion caused by the disease or inflammation caused by topical remedies (counterirritant ointments or lotions or strong ultraviolet rays) the biologic effect of the radiation is greater than is anticipated. Such congestion or inflammation may mask a slight acute radiodermatitis with resulting unexpected radiation sequelae. Errors are also made in forcing the issue with radiation therapy: If certain cases of eczema, psoriasis and other dermatoses do not respond to an adequate amount of radiation, the continuance of such treatment may lead to therapeutic fastness or radiodermatitis.

Many cases of radiodermatitis and other undesirable radiation reactions result from the improper protection of normal tissue from scattered and secondary radiations. Such areas as the hairy parts, eyes or testes should be protected with suitable opaque materials in all instances. Overdosage may result from crossfiring, back scattering and overlapping of rays. The inadvertent omission of the filter or the improper selection of the filter when administering a radium or x-ray treatment accounts for some cases of radiation sequelae. Radiodermatitis may also result from haphazard guesswork in dosage determination, from faulty diagnosis, from repeated treatment of recurrences and from failure to obtain a history of previous treatments with radium or x-rays. The application of radium or radon over an area that was previously repeatedly examined with x-rays or by fluoroscopy may lead to a radiodermatitis. Perhaps the greatest harm is done with radium by using it when not indicated or as an unnecessary aid to other treatment.

A physician who uses x-rays or radium for treating dermatologic conditions should be a dermatologist or should be guided by one. The necessity for this attitude is best illustrated as follows: A patient may complain of anal pruritus. The diagnosis of essential pruritus ani should be confirmed. Such possible causes as a fungus, diabetes, intestinal parasites, anorectal disorder, allergic conditions or neurodermatitis should be eliminated. If it is assumed that the condition is essential pruritus ani and an adequate amount of irradiation fails to relieve it, then it is unlikely that additional treatment will be effective. The indications, the contraindications, the response of certain diseases to a given quantity of radiation, the tissue response and the natural evolution and involution of dermatoses are best understood by dermatologists. It is also important that the dermatologist who uses radiation be thoroughly familiar with all phases of radiation that apply to the treatment of cutaneous diseases. The details of acute and chronic radiodermatitis may be found in standard textbooks.³

I hope that it has been sufficiently emphasized that the proper administration of radium, radon or x-rays in the treatment of cutaneous diseases requires specialized training in both dermatology and radiology. Also that company physicists are not qualified to advise dermatologists or radiologists in the proper use of radium. Especially is it poor practice to obtain advice from company physicians and physicists regarding technic, filtration, dosage, method of administration of radium or radon without the consulting physician or physicist seeing the patient. The practice of telephone and mail consultation is particularly undesirable.

40 East Sixty-First Street.

3. MacKee, George M.: *X-Rays and Radium in the Treatment of Diseases of the Skin*, Philadelphia, Lea & Febiger, 1939.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.
PAUL NICHOLAS LEECH, Secretary.

THE PRESENT STATUS OF THE GONADOTROPIC HORMONE FROM THE SERUM OF PREGNANT MARES: GONADOGEN (THE UPJOHN COMPANY), ANTERON (SCHERING CORPORATION) AND GONADIN (CUTTER LABORATORIES) NOT ACCEPTABLE FOR N. N. R.

The gonadotropin obtained from the serum of pregnant mares is being actively marketed at the present time for therapeutic purposes. The Upjohn Company claims that its preparation of pregnant mares' serum (Gonadogen) is useful in males with hypogonadism of pituitary origin, in oligospermia and sterility, and in females for menstrual irregularities, functional bleeding, certain types of dysmenorrhea, sterility and failure of ovulation.

Schering Corporation recommends Anteron, a similar preparation, in the treatment of amenorrhea, functional bleeding and hypogonadal sterility in females, and sterility and hypogonadism in males.

Gonadin is advertised by Cutter Laboratories to be indicated in amenorrhea, functional bleeding, sterility in the female and disorders of sperm formation in the male.

On theoretical grounds, gonadotropic hormone from serum of pregnant mares appears to possess several desirable physiologic properties which might be enlisted for therapeutic purposes:

1. It is capable of inducing ovarian growth in primates, in contrast to chorionic gonadotropin (from human pregnancy urine), which is unable to affect such ovaries in this regard.
2. It stimulates the germinative epithelium of the ovaries and testes in laboratory animals.
3. Its physiologic properties resemble those of the anterior lobe gonadotropic factors.
4. It can be prepared for commercial purposes in a more concentrated and purer form than gonadotropic extracts of the anterior lobe.

It has been fairly well demonstrated that mare serum gonadotropin is effective in inducing some degree of ovarian growth in human beings. Westman¹ reported that seven women responded with an increased growth of the follicular apparatus, which in five cases he considered excessive. Moricard and Saulnier² likewise stimulated follicular development with a similar preparation in several women.

In 1938 Davis and Koff³ reported that they had induced ovulation in women with the mare serum gonadotropin administered intravenously. No one, up to this time, had succeeded in producing this reaction. The work of these investigators aroused great interest in this preparation, and the application of such therapy to certain gynecologic disorders was held most promising. These authors recognized the possibility, however, that ovulation might be induced in this manner only in women with normal ovaries, which would, of course, limit its therapeutic application. Up to the present time the work of Davis and Koff has been confirmed only by Siegler and Fein.⁴ On the other hand Hartman,⁵ working with a large number of monkeys, could induce only infrequent ovulations by mare serum gonadotropin injections (7 per cent of 104 animals). He observed varying degrees of ovarian stimulation in most of his animals, but a considerable number remained refractory. The

1. Westman, A.: Untersuchungen über die Wirkung des gonadotropen Antex (Leo), auf die Ovarien der Frau, *Arch. Gyn. u. Obst.* **17**: 492, 1937.

2. Moricard, F.: Développement folliculaire provoqué par l'injection de sérum de jument gravide, *Bull. Soc. gynec. et obst.* **27**: 132 (Feb.) 1938.

3. Davis, M. E., and Koff, A. K.: The Experimental Production of Ovulation in the Human Subject, *Am. J. Obst. & Gynec.* **36**: 183 (Aug.) 1938.

4. Siegler, S. L., and Fein, M. J.: Studies in Artificial Ovulation with the Hormone of Pregnant Mares' Serum, *Am. J. Obst. & Gynec.* **38**: 1021 (Dec.) 1939.

5. Hartman, C. G.: The Use of Gonadotropic Hormones in Adult Rhesus Monkey, *Bull. Johns Hopkins Hosp.* **63**: 351 (Dec.) 1938.

stimulation consisted chiefly of follicular enlargement and only an occasional corpus luteum.

Among the conditions which appeared, on theoretical grounds, to be suited to therapy with this form of gonadotropin were those in which there was a failure of ovulation. Certain cases of amenorrhea, oligomenorrhea and menorrhagia are included in this category. Functional sterility in some patients is also supposed to result from a defective ovulation mechanism. Successful treatment of the latter condition would, of course, be a great boon to these childless couples. Whether or not the ovum from such an artificially induced ovulation would be normal at all times remains to be demonstrated. Other suggested indications are menstrual dysfunctions due to abnormal follicular development and some types of testicular dysfunction, including defective sperm formation.

The reports on the clinical trials with this substance have been, unfortunately, rather unsatisfactory to date. Bowes⁶ reported satisfactory results in regulating the menses in four out of five patients. Kennedy and Shelton⁷ have likewise reported beneficial responses in three cases of menorrhagia and eleven cases of amenorrhea. The data in these reports were clinical only. The recent report of Hall⁸ disclosed extraordinary results in a large group of patients (135). Eight of seventeen patients with genital hypoplasia were reported "cured," twenty-four of forty-three sterile women became pregnant, and 57.6 per cent of those with menstrual disturbances were also "cured." This work requires confirmation, since no other investigators have approached the success of Hall and since no objective evidence was presented by this investigator. Severinghaus and his associates⁹ have used gonadotropic hormone from serum of mares in both males and females with encouraging results.

The investigations of Gray¹⁰ are the first to include laboratory data which demonstrate the effect of the mare gonadotropic substance on the reproductive tract of women with menstrual disturbances. This worker at intervals took biopsies of the endometrium of his patients before and after therapy was instituted. In four of eleven cases of secondary amenorrhea the endometrium was changed to the secretory type after two to thirteen months of treatment. Eight of the eleven patients responded with regular menstruation or "fairly so." In seven cases of menorrhagia with endometrial hyperplasia bleeding was unchecked after one to sixteen months of treatment, and there was little effect on the endometrium. In seven cases of metrorrhagia, two responded with regular menstruation. The others were not significantly affected, and only one endometrium was altered to the premenstrual type. In six patients with "minor metrorrhagia" there was improvement in only one.

Gray questioned Hall's results in treating functionally sterile women: "One is led to presume that 55 per cent [twenty-four of forty-three] of cases with sterility, at least in that series, were due to failure of ovulation. In our opinion sterility due to failure of ovulation in a woman with normal, regular menstrual periods is a distinct rarity."

In the male, Kunstadter¹¹ has reported satisfactory results in cryptorchism and hypogonitism in boys treated with mare gonadotropin, but there appears to be, from his results, no advantage for this therapy over that with chorionic gonadotropin. Recently Rowlands and Spence¹² have shown that mare serum gonadotropin was rather unsatisfactory in the treatment of cryptorchism. Furthermore, a state of refractoriness was induced when this substance was administered for several weeks, which appeared to be due to the development of an antigonado-

tropic substance. No competent studies on the treatment of other disorders of the male gonads (including sterility) with mare gonadotropin are available to date.

The evidence in the literature, which forms the basis of this report, except for several lesser references, is definitely inadequate as a basis for the recommendation of therapy with mare gonadotropin. Our knowledge of the physiologic and pathologic action in primates, especially man, is still most uncertain. Certainly there is little justification for claims of consistent therapeutic success in gonadal disorders on the basis of the physiologic reactions obtained in laboratory animals and the meager clinical data reported up to the present time. It is apparent that adequate investigations from the laboratory standpoint, which should include endometrial biopsies, hormonal assays, vaginal smears and chemical studies, are essential for the proper evaluation of the effect of this gonadotropic substance on the abnormal as well as the normal human ovary, and secondarily on the accessory sex organs.

Further experimentation is obviously required under suitable conditions and by investigators whose special training qualifies them for the appropriate study of this material. Until the time when the status of gonadotropin from serum of pregnant mares may be properly evaluated, physicians are cautioned that the use of this substance is still in the early experimental stage, that the claims made by the manufacturers are without satisfactory foundation, and that additional publication of more satisfactory evidence is necessary before this substance should be used in routine practice.

The Council, therefore, voted that the preparations of gonadotropin from serum of pregnant mares marketed as Anteron (Schering Corporation), Gonadogen (the Upjohn Company) and Gonadin (Cutter Laboratories) be declared unacceptable for inclusion in N. N. R., since their advertising claims for its therapeutic use are based on an insufficient amount of scientific evidence and inadequate confirmation of reported results. The right, under the Council's rules, of any firm to the use of a proprietary name for this substance was not considered at this time.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

ALLERGENIC EXTRACTS-MULFORD (See New and Nonofficial Remedies, 1940, p. 32).

The following additional products have been accepted; they are marketed in 5 cc. ampule vials:

Products marketed in dilutions representing 0.005 mg. of nitrogen per cubic centimeter:

*Rat Hair.*⁴

Products marketed in dilutions representing 0.05 mg. of nitrogen per cubic centimeter:

Allspice,¹ Aniseed,¹ Caraway Seed,¹ Cashew Nut,¹ Gelatin (Cattle),¹⁹ Hazelnut,¹ Hops,² Horse-Radish,² Mace,² Pimento,² Poppy Seed,¹ Sage,¹ Tapioca,¹ Thyme.¹

Products marketed in dilutions representing 0.25 mg. of nitrogen per cubic centimeter:

Curran,² Pigeon Feathers,⁴ Turkey Feathers.⁴

Products marketed in dilutions representing 0.5 mg. of nitrogen per cubic centimeter:

Anchorvy,² Butterfish,² Castor Bean,¹¹ Catfish,² Chickory,¹ Date,² Lime,² Pike,² Poroy,² Quince,² Sardine,² Weakfish,² Whitefish.³

Product marketed in a dilution representing 0.75 mg. of nitrogen per cubic centimeter:

Feathers Mixed (Chicken, Duck and Goose).⁴

Castor Bean, marked 11, is prepared for extraction as follows:

The material is ground and washed with toluene and ether until the washings are colorless. The residue is extracted with buffered salt solution for seventy-two hours at room temperature. The extract is boiled for three minutes and filtered through a Mandler candle.

MAGNESIUM TRISILICATE (See THE JOURNAL, April 6, 1940, 1355).

The following dosage form has been accepted:

Tablets Magnesium Trisilicate, 0.324 Gm. (5 Grains).
Prepared by the Smith-Dorsey Co., Lincoln, Neb.

6. Bowes, Kenneth: Treatment of Menstrual Irregularities by a New Sex Hormone Preparation: Preliminary Note, *Brit. M. J.* 2: 904 (Nov. 6) 1937.

7. Kennedy, R. B., and Shelton, C. F.: The Mare Serum Hormone in the Treatment of Certain Endocrine Dysfunctions in Women: A Clinical Study, *J. Michigan M. Soc.* 38: 209 (March) 1939.

8. Hall, G. J.: Gonadotropic Hormone of Pregnant Mares' Serum: Its Clinical Use in Gynecology, *California & West. Med.* 51: 159 (Sept.) 1939.

9. Severinghaus, Elmer L.: Treatment of Gonadal Hypofunction, *Bull. New York Acad. Med.* 16: 53 (Feb.) 1940.

10. Gray, L. A.: Effect of Pregnant Mares' Serum Hormone on the Abnormal Ovary, *South. M. J.* 33: 160 (Feb.) 1940.

11. Kunstadter, R. H.: The Treatment of Hypogonitism in the Male with the Gonadotropic Principle of Pregnant Mares' Serum, *Endocrinology* 25: 661 (Nov.) 1939.

12. Rowlands, I. W., and Spence, A. W.: Production of Antigonadotropic Activity in Man by Injection of Extract of Pregnant Mares' Serum, *Brit. M. J.* 2: 947 (Nov. 11) 1939.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 7, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

LIFE-SAVING SERVICE WITHOUT RECOGNITION

The disaster to the U. S. S. *Squalus*, the submarine from which a considerable number of lives were salvaged, is no doubt still fresh in the minds of many American citizens. Few people realize, however, the part played by the Medical Corps of the United States Navy in the saving of life in this catastrophe. Early in June 1939 the submarine *Squalus* dived to the bottom and did not come up. Apparently water had rushed into the submarine, and twenty-six men who had been locked in the flooded compartments perished. In the forward compartments were thirty-three men who still lived. Twenty-four hours after the *Squalus* sank the Navy had its experts and rescue devices on the scene. Divers went down in a diving bell, slid a shackle over a ring on the deck of the submarine and attached a cable. Then the rescue bell was clamped over a hatch on the sunken ship, the hatch was opened, and one

officer and six seamen climbed into the bell and were raised to the surface. By this process, in a period of eight hours every living man aboard the *Squalus* was taken into the bell. Except for an accident which occurred on the final trip, all were released in that time. One officer and seven men were held in the bell by a jamming of the cable, which, however, was finally cut so that all were rescued.

The saving of the men on the *Squalus* was possible largely because of some extraordinary scientific investigations made by members of the United States Navy Medical Corps in the years since 1932. In those investigations Lieut. Albert R. Behnke contributed notably. A series of papers has been published in the *United States Naval Medical Bulletin*. These investigations, which are concerned with a determination of the cause of accidents with the submarine escape apparatus, the narcotic action of nitrogen, the development of the use of helium, improvements in decompression tables, the development of an effective method of utilizing oxygen in the treatment of air embolism and the discovery that the diffusion of helium through the skin may be used as a measure of peripheral circulation are all fundamental contributions, on which rescue work such as that involved in the saving of the men on the *Squalus* must be based.

Significantly, in all of these investigations, involving more than twenty-five individual contributions to scientific medical literature, the physicians have themselves submitted to various tests before any enlisted men were permitted to volunteer for such a purpose. The value of their work is shown by the fact that only two minor cases of bends developed out of 640 dives, whereas bends occurred almost daily in previous rescue work even though the depths were much less.

The story of the salvaging operations on the U. S. S. *Squalus* was published in the *United States Naval Medical Bulletin* for October 1939. The *Squalus* disaster provided a crucial test for the preparation which Navy medical officers had made over a long period of time. The medical discoveries already mentioned were supplemented by some engineering innovations involving the fabrication of fireproof, electrically heated garments for cold-water diving, improved recirculation of gas through the diver's helmet and the perfection of telephone communication. Indeed, these also were medical as well as engineering problems before they were finally perfected by the engineers. It was found that diving in semidarkness to a depth of 240 feet for the purpose of tunneling under the submarine and attaching the hoses was too dangerous when divers breathed air. The accumulation of carbon dioxide and nitrogen narcosis impaired neuromuscular coordination to such an extent that simple tasks could be carried out only with great difficulty. The substitution of helium for nitrogen in the air minimizes the narcotic symptoms associated with air breathing under pressure. Substitution of oxygen for air or a helium-oxygen mixture in the lungs allows

excess nitrogen or helium gas to diffuse from the body at a maximum pressure head.

The complete story of the *Squalus* disaster and the rescue has not yet, of course, been told. At this time, however, not one of the three medical officers in attendance on the *Squalus*, including Lieuts. Oscar D. Yarbrough, Albert R. Behnke and Thomas L. Willmon, has been given any special award in recognition of his performance. With the exception of two pharmacist's mates, none of the Hospital Corpsmen who worked in this disaster have been recognized by an award. Nevertheless, practically every other officer and Naval "rating" who took part in the salvage has apparently been given special recognition. The reticence of the medical profession in seeking rewards for such service is proverbial. In this instance, when the attention of all the world was focused on the plight of the men who sank in the *Squalus*, when it is recognized that only years of preliminary efforts on the part of medical investigators in the United States Navy made possible the salvaging of those who were saved, when it is recognized that these men in person and the Hospital Corpsmen who were associated with them were in attendance on the actual salvaging operation, neglect to give them the type of special award given to the nonmedical personnel is so evident as to demand this statement. Organizations which know how to impress their opinions on government officials might well adopt official actions to indicate their belief in the justice of the claims of these men to governmental recognition.

SELENIUM AND DIETARY PROTEIN

Within the past few years the etiology of "alkali disease," a condition affecting horses, cattle, swine and poultry of certain areas of South Dakota, Nebraska and Wyoming, has been elucidated.¹ Wheat, corn and barley grown on soils of these areas contain selenium, a chemical cousin of sulfur; this element is definitely associated with the protein fraction of "toxic" grain.² A preliminary report recently announced the actual isolation from seleniferous plant material of a crystalline organic compound containing selenium and having the properties of an amino acid.³ Selenium also occurs in body protein of animals fed for long periods on selenized grains.⁴ This selenium behaves in some respects like that found in proteins of selenized grain, and possibly the toxic element is present in a similar chemical combination in both cases.

As persons living in areas where "alkali" disease is endemic also ingest food containing selenium, it seemed possible that chronic selenium poisoning might also be

encountered in residents of these areas. Nevertheless, despite the fact that persons in selenium-endemic areas may consume this substance in food up to 0.2 mg. per kilogram of body weight daily, convincing evidence of serious chronic selenium poisoning from this source has never been reported in man.⁵ A possible explanation of this situation is afforded by the observation that in animals the toxicity of selenium which is chronically ingested in food is influenced greatly by dietary factors.⁶ It has been found, for instance, that an amount of selenium which will cause extensive tissue damage to animals on a diet low in protein and high in carbohydrate will do little or no harm to animals maintained on diets high in protein and low in carbohydrate. Moreover, not only the toxicity of naturally occurring food selenium but also the toxicity of sodium selenite is influenced by the amount of protein in the diet.⁶

Smith⁵ has pointed out that the toxicity of selenium in food seems to be determined within certain limits by the ratio of selenium to protein in the diet rather than by the level of selenium in the food as heretofore supposed. This aspect of the selenium problem has been confirmed and extended in a recent report by Gortner,⁶ who observed that the quality as well as the quantity of protein in seleniferous diets assumes a role in determining the toxicity of selenium. Casein and lactalbumin tend to counteract the toxicity of selenium, for instance, while edestin and gelatin are not effective in this respect. These recently discovered relationships between the toxicity of selenium in food and the quality and quantity of the protein in the diet have an important bearing on the question of selenium as a health hazard to man and they serve to emphasize once more the fundamental importance of good diets in the maintenance of public health.

Current Comment

TEACHING OF SOCIAL MEDICINE

According to a recent study "A total of 715 courses covering one or more topics on social medicine was offered by 139 colleges and universities."¹ In addition there were more than a thousand courses in which one or more lectures were devoted to some aspects of social medicine. The 715 full and part courses were analyzed as to the frequency of the topics included. Thus, 432 courses treated "social and economic problems affecting public and individual health," 295 dealt with "health insurance, general," 180 with "voluntary health insurance," and 37 with "compulsory health insurance." There were 112 full courses on social medicine given at sixty-three colleges and universities. These are scattered through a variety of departments, some of which would

1. Selenium Problem, editorial, *J. A. M. A.* **104**: 50 (Jan. 5) 1935; Toxic Effects of Selenium, *ibid.* **106**: 926 (March 14) 1936.

2. Horn, M. J.; Nelson, E. M., and Jones, D. B.: Studies on Toxic Wheat Grown on Soils Containing Selenium, *Cereal Chem.* **13**: 126, 1936.

3. Horn, M. J., and Jones, D. B.: Isolation of a Crystalline Selenium-Containing Organic Compound from Plant Material, *J. Am. Chem. Soc.* **62**: 234 (Jan.) 1940.

4. Westfall, B. B., and Smith, M. I.: The Distribution of Selenium in Plasma and Liver Proteins and Its Fractionation in Tryptic Liver Digests, *Pub. Health Rep.* **55**: 1575 (Aug. 30) 1940.

5. Smith, M. I.: The Influence of Diet on the Chronic Toxicity of Selenium, *Pub. Health Rep.* **54**: 1441 (Aug. 4) 1939.

6. Gortner, R. A., Jr.: Chronic Selenium Poisoning as Influenced by Dietary Protein, *J. Nutrition* **10**: 105 (Feb. 10) 1940. Smith.⁵

1. Hirsh, Joseph, and Pritchard, Elizabeth G.: Teaching of Social Medicine in Liberal Arts Colleges and Universities, *Pub. Health Rep.* **55**: 2041 (Nov. 8) 1940.

seem to be scarcely related to the subject. Twenty courses are in the department of biologic sciences, thirty-eight in physical education and hygiene, twenty-seven in social work and thirteen in sociology. None of the courses were found in departments of economics and history. Comments would seem to indicate that the courses given in the departments of biologic sciences and physical education and hygiene place the emphasis on treatment of individual and social health rather than on broader questions of policy in the organization of medical services. The fact that 512 full or part courses deal with some phase of health insurance arouses curiosity as to the extent to which such courses are descriptive and analytic and how much of them are propaganda. The fact that little use has been made in any of these courses of the material on these subjects in the Bureau of Medical Economics of the American Medical Association may indicate that most of the information placed before students is derived by prejudiced instructors from private, foundational and governmental propaganda institutions and is largely colored by these sources.

THE POST HAS NEVER SEEN A VITAMIN!

An advertisement for the *Saturday Evening Post*, November 27, was headed "Two Things You Never Saw Photographed." More than half of the advertisement is a reproduction of an f:6.3 Eastman anastigmat lens, with the following text:

In a Dutch prison in Java over thirty years ago, a young medical officer noticed that prisoners eating polished rice were suffering. Then he made the discovery that the trouble was caused not by something *present* in the rice, but by something *absent*—something hidden in its silvery skin. Something we now call a vitamin.

Scientists have traced a dozen evils to missing vitamins—from beriberi to night blindness. They know that some foods are rich in vitamins. And some are not. But you never saw a *picture* of a vitamin, did you?

If the writers of the *Saturday Evening Post* advertisement had consulted the many vitamin research laboratories, both in the industry and in academic circles, they would have seen photographs aplenty of vitamins—not only of thiamine (in the form of thiamine hydrochloride), the lack of which causes beriberi, but pictures of crystals of vitamin A, of nicotinic acid, riboflavin (vitamin B₂), pantothenic acid, ascorbic acid (vitamin C), the crystalline vitamin D compounds and a number of others. They even used for the illustration a 6.3 lens, when amateur photographers would have known better. Perhaps this incident reflects what is wrong with much so-called scientific copy. The writers are more interested in the "idea" than in scientific accuracy. They could have found, by a very small amount of research first, that many vitamins have been isolated in crystalline form; second, that there are many potent substances that have never been seen. There is the "something" that causes a cancer cell to assume malignancy; there are viruses of a number of serious diseases; there is the "something" that makes men go to war; and then finally there is the birth of an idea. These thoughts we present to the agency with no thought of further recompense than the joy of giving; and that cannot be measured either.

NATIONAL PHYSICIANS' COMMITTEE

Many inquiries have been received relative to a mailing which the National Physicians' Committee for the Extension of Medical Service has just sent, we are informed, to every physician in the United States. In this statement of its postelection position, policy and program, attention is called to the statements made by President Franklin D. Roosevelt and Mr. Wendell Willkie on the subject of socialized medicine previous to the election. The committee points out the importance of sustaining public opinion so that the public will come to understand the vital importance of maintaining the delicate and subtle relationship of doctor and patient and will support the independence of the medical profession. At a meeting of its Management Committee, held in Chicago on November 10, the National Physicians' Committee, says the statement, adopted the following resolutions:

Be it recorded that it is the unanimous opinion of the Management Committee of the National Physicians' Committee that under conditions now prevailing there is a greater and more pressing need than at any previous time for such activities as those of the National Physicians Committee.

Be it recorded as the unanimous opinion of the Management Committee that we continue the operations of the National Physicians Committee with increased vigor.

With this decision the National Physicians' Committee has sent to the medical profession a list of activities and objectives proposed for the coming year and a plan for sustaining the organization so that it will be able to function effectively. This statement follows:

NATURE OF ACTIVITIES AND OBJECTIVES

It is essential that funds be provided for:

1. A continuous flow of articles to more than eighty medical journals.
 2. Stimulating discussion of this all-important issue in forty-eight state medical meetings, in the meetings of two thousand county medical societies, and hundreds of sectional and special medical meetings and conferences.
 3. Preparing and providing for the preparation of articles and releases for thousands of newspapers and hundreds of magazines, and arranging for their publication.
 4. Speakers for medical and public meetings and arranging for physicians appearing before local groups and on local radio broadcasts.
 5. Radio broadcasts and the preparation of speeches and radio broadcasts to be generally available, and the providing of electrical transcriptions of short speeches and radio broadcasts and arranging for their effective use.
 6. The maintaining of strategically important public contacts.
 7. The arranging of conferences with boards of hospitals and clinics; business, industrial and other lay groups; and for group meetings of laymen.
- all to the end that:
- (a) political control of medicine can be avoided;
 - (b) the independence of the profession and the pattern of medical practice be preserved; and,
 - (c) the American people can be resold on the incomparable advantages of the American Way of Life.

The medical profession generally has been asked to contribute to a furtherance of these commendable objectives. The work of the National Physicians' Committee, which is wholly in charge of its own Board of Trustees, thus contemplates an expanded program of public enlightenment. Since new legislation in the field of medical service is constantly before Congress, an agency of this type will find a large field for its service.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

THE 1940-1941 MILITARY TRAINING PROGRAM

Participation of the Medical Department of the Army

Uppermost in the minds of all physicians at present is undoubtedly the question of national defense. The medical departments of the armed forces must plan to meet the immediate twofold problem of furnishing an adequate medical service to the men of our unprecedented peacetime Army and Navy, and of training the large number of Medical Department trainees who, at the expiration of their twelve months military service, will pass to the Enlisted Reserve Corps. They will furnish the trained personnel required for mobilization in the event of a national emergency. The Surgeon General of the Army has furnished the following outline regarding the participation of the Medical Department of the Army in the 1940-1941 military training program:

THE NEED FOR PERSONNEL

The total strength of the army of the United States next spring will be approximately 1,400,000. This represents a Regular Army of 400,000 officers and men, the National Guard of the several states federalized as the National Guard of the United States, numbering 200,000, and citizens selected for military training during the coming twelve months—about 800,000 in number. The latter will receive their training in active units of the Regular Army and of the National Guard, in Regular Army inactive units activated for training purposes, in the numerous installations required for the overhead of these forces and in enlisted replacement centers throughout the nine corps areas of the country.

PROVISION OF HOSPITAL BEDS

The Medical Department is charged with providing adequate medical service for the entire army of the United States at posts, camps and stations within and beyond the continental limits of the United States. In each military station in the United States there will be a hospital with four beds for each hundred of the military population. The operating room, kitchen, messing facilities and clinics in each of these hospitals will be of sufficient size to provide service for an additional patient per hundred men so that in an emergency it will be necessary to construct only the additional ward buildings. Furthermore, there will be general hospitals suitably located throughout the United States to provide an additional bed per hundred of the military population.

The provision of 5 per cent of hospital beds which can be rapidly expanded to 6 per cent may appear excessive when compared with hospitalization provided for the civilian population of this country. However, all of the military sick, including such cases as in civilian life are ordinarily cared for in their homes, must be treated in hospitals, since they cannot receive satisfactory care in the barracks. In addition, when young adults are brought together in large groups, contagious and infectious diseases that spread rapidly under such conditions occur much more frequently than in civil life. Furthermore, sufficient beds must be provided for

the care of the sick during the winter and spring seasons of the year, when there is always an excessive number of such cases.

Scattered throughout the large camps or stations there will be dispensary buildings and dental clinics for the infirm care and dental treatment of the personnel. In addition, in each large camp there will be a medical headquarters, with properly qualified scientists for the general supervision of the medical activities, including the protection of the health of the troops, the careful inspection of food products and the general supervision of the nutrition of the men.

The Medical Department will be charged with the training of the medical detachments and the medical department units of the Regular Army and the National Guard, and with the instruction of the service personnel in hospitals and other installations. It is also responsible for the preparation of the trainees in enlisted replacement centers, in hospitals and in service schools, who will receive there the individual Medical Department instruction which will permit their incorporation in organizations for further unit training.

REQUIREMENT OF PHYSICIANS

The initial requirement will be approximately 6.5 doctors for each thousand men in the military service. Rapid calculation will show that the total number for an army of 1,400,000 men will be 9,100 doctors. Additional ones may be required, but in the interest of economy the initial procurement will be limited to the number stated. The 1,200 physicians in the Regular Army and the 1,100 in the National Guard are included in the total, leaving approximately 6,800 physicians to be supplied by the Reserve Corps. There are now in active service or under orders approximately 1,500 Reserve physicians, leaving 5,300 to be procured during the next few months.

STATUS OF THE RESERVE CORPS

Under the recent joint resolution passed by the Seventy-Sixth Congress, the President is authorized to order into the active military service of the United States for a period of twelve consecutive months each any or all members of any Reserve component of the Army of the United States, with or without their consent, to such extent and in such manner as he may deem necessary for the strengthening of the national defense. If a sufficient number of officers do not indicate their availability for this service, Reserve officers must necessarily be ordered to duty without their consent. Additional appointments among physicians of draft age will increase the strength of the Medical Corps Reserve. However, it is apparent that a large percentage of these officers must participate actively in the present program for preparing a portion of the country's man power for national defense.

In establishing rosters from which officers will be ordered to duty, corps area commanders and chiefs of

branches have been instructed to circularize all Reserve officers under their assignment jurisdiction to permit them to state the amount of deferment desired and the cogent, pertinent reasons for such deferment in the event that they are not immediately available for military service. This action has been taken in view of the fact that a national emergency has not been declared by the Congress, nor has mobilization been ordered. The medical service of a training program, although essential to national preparedness, possesses none of the glamour of the same service during actual military operations; it is, however, equally important. Indeed, military training may, through the thoroughness of its preparation for war, materially assist in preventing the necessity of participation in military operations. It is realized, of course, that all officers would express their immediate availability in the event of war; many, however, feel that their services are not of national importance at the present time.

Both the economic and the rational utilization of medical officers is essential. It is planned that as far as possible qualified officers will be selected for assignment to duty with units and at installations according to their previous training and experience. Accordingly, selection must be qualitative as well as quantitative in order that the specific requirements of a modern medical service may be properly met. Officers selected for duty will be given the maximum possible advance notice of such action.

INFORMATION FOR MEDICAL RESERVE OFFICERS ORDERED TO DUTY

In this connection the Surgeon General has suggested that the following points be brought to the attention of all Reserve medical officers:

1. When notified that you have been selected for active duty, submit at once the required report of physical examination. The disclosure of disqualifying

Pay and Allowances of Medical Reserve Officers

Grade	Annual Base Pay	Allowances			
		Rental Allowance		Subsistence Allow- ance (30 Days)	
		With Depen- dents	Without Depen- dents	With Depen- dents	Without Depen- dents
Colonel.....	\$4,000	\$120	\$80	\$36	\$18
Lieutenant Colonel..	3,500	120	80	54	18
Major.....	3,000	100	60	54	18
Captain.....	2,400	80	60	36	18
First Lieutenant.....	2,000	60	40	36	18

defects prior to the issuance of orders may prevent a disruption of your practice or civil employment.

2. Orders issued will place you on active duty at your home or, if a temporary change of address has been submitted, at that location, and will direct you to report to a specific post, camp or station for duty.

3. Travel to your station may be accomplished by automobile, but no delay will be granted for that purpose above the customary time for travel by rail.

4. You will be reimbursed for travel at the rate of 8 cents a mile, based on the shortest usual railway route to your station.

5. Transportation for dependents to your first station will not be furnished by the government. It is perhaps advisable that your family not accompany you, since the housing problem at or within the vicinity of Army stations is frequently acute.

6. If you have no uniform and military equipment, these may be purchased at your first station.

7. Pay and allowances are as shown in the accompanying table.

The annual base pay is increased at the rate of 5 per cent thereof for each three years of service up to thirty years. Full time will be computed for all periods during which men have held commissions as officers in the Army, Navy, Marine Corps, Coast Guard, Coast and Geodetic Survey and Public Health Service, or in the National Guard or Naval Militia, the National Naval Volunteers or the Naval Reserve Force or Marine Corps Reserve, when confirmed in grade and qualified for all general service, and with full time for all periods during which they have performed active duty under Reserve commissions, and with one-half time for all other periods during which they have held Reserve commissions.

PHYSICIANS UNDER SELECTIVE SERVICE

Physicians as a group will not be exempt from conscription for military training and service. Their deferment because of importance to civil communities is a function of the local draft boards. Accordingly, it is difficult to approximate the number which will be inducted into the Army. Obviously, the training received by such draftees will be more appropriate and the services rendered the Army of greater value if the physicians who are eligible and qualified for appointment in the Medical Corps Reserve be commissioned in the Officers Reserve Corps for duty as medical officers, rather than continue their training as enlisted men.

Physically qualified graduates of approved schools of medicine who desire appointment in the Medical Corps Reserve for immediate active duty should make application to the commanding general of the corps area in which they reside. Such applications may be submitted either before or after selection for military training and service or after induction into the Army of the United States. No change in the classification of such applicants will, however, be made by local selective service boards until the actual letter of appointment has been received.

APPOINTMENTS IN THE MEDICAL CORPS

Appointments in the Medical Corps of the Regular Army will, in all probability, continue as at present through competitive examinations of Reserve officers who have not passed the age of 32 years at the time of appointment.

WORK OF THE AMERICAN MEDICAL ASSOCIATION

The Surgeon General of the Army, through Lieut. Col. George C. Dunham, the representative of the Medical Department in the House of Delegates, submitted a request to that body at its last meeting in New York, in June 1940, requesting the assistance of the American Medical Association in the classification and procurement of physicians for the Army. It was hoped in this way to procure the physicians required without disturbing too seriously the civilian medical service and at the same time to place the physicians enrolled in positions for which their previous training qualified them. The House of Delegates approved the request of General Magee and appointed a Medical Preparedness Committee. The U. S. Navy and the U. S. Public Health Service made similar requests.

Reference has been made to the action of the House of Delegates and to the working of the Preparedness Committee in previous issues of THE JOURNAL. The Preparedness Committee, the executive officers of the American Medical Association and the chairman and

members of the various state and local committees have all given generously of their time and funds in this work. They have been of material assistance to the Surgeon General and corps area surgeons in the classification and procurement of Reserve Corps medical officers. They generously have offered their assistance in similarly classifying and procuring such physicians as may be required in addition to those in the Reserve Corps. Although the majority of appointments of additional Reserve officers for active duty at this time will be 35 years of age or under, a limited number of properly qualified physicians above this age will be required as chiefs of services of the many large hospitals to be established.

COOPERATION OF MEDICAL PROFESSION

The history of our country has repeatedly shown that there is no more patriotic group than the American physicians. They have always responded generously to

their country's call for assistance. At this time, although this country is not engaged in war, the national preparedness program requires an adequate medical service. Without it, the program will be hampered materially. In addition to the adequate care of the sick and protection of the health of our young men in the camps, the Medical Department must be able to train its personnel to act in conjunction with the troops of the other arms and services so that in time of battle, if unfortunately that time should come, it may be able to collect efficiently and evacuate promptly casualties that occur on the battlefield so that each one may receive as promptly as possible efficient medical care. Let us repeat: The success of the national preparedness program depends to a large extent on adequate medical service. American medicine appreciates its obligations and will furnish a sufficient number of properly qualified physicians.

CONFERENCE ON MEDICAL PREPAREDNESS HELD AT AMERICAN MEDICAL ASSOCIATION HEADQUARTERS, SATURDAY, NOV. 23, 1940

The following were in attendance:

Dr. Irvin Abell, chairman, presiding.	Brig. Gen. A. G. Love.
Dr. James A. Crabtree.	Dr. John H. O'Shea.
Dr. Charles A. Dukes.	Dr. Stanley H. Osborn.
Lieut. Col. George C. Dunham.	Dr. James E. Paullin.
Dr. Morris Fishbein.	Dr. Walter G. Phippen.
Dr. Roy W. Fouts.	Lieut. Col. C. B. Spruit.
Lieut. Col. C. G. Hutter.	Dr. Harvey B. Stone.
Dr. R. G. Leland.	Dr. Nathan B. Van Etten.
	Dr. Olin West.

FORENOON SESSION

Communications were read from Dr. Frederick Rankin of Kentucky and Dr. Samuel E. Thompson of Texas, who were unable to be present.

Remarks on Progress by Corps Area Representatives

Dr. Paullin said that the problem at present in the Fourth Corps Area concerned the distribution of physicians in counties where there were few doctors. They are preparing in those counties for medical care. Problems have arisen in North Carolina, South Carolina and Georgia concerning medical reserve corps officers who have been called into service with the possibility that their communities will lack sufficient medical service. An attempt has been made to settle the problem in each state and Dr. Paullin stated that Georgia has settled it. The second problem in the Fourth Corps Area is that of residents in teaching hospitals where some have been ordered to active duty; the suggestion has been made that they can operate as well with a slightly diminished personnel if those who remain will do a little more work. Through the state and local chairman, all members of the profession are being listed as to whether they can be spared from their communities and the lists are to be given to the corps area surgeons. The medical preparedness organizations have not as yet been functioning well in North Carolina and South Carolina.

Dr. Osborn and Dr. Phippen said that in the First Corps Area they have given the selective service and the local recruiting office all the assistance they have asked for in the way of induction and draft board physicians. A problem that confronts them in Massachusetts in completing the survey questionnaire is that of 2,400 nonmembers of the Massachusetts Medical

Society, including a lot of men from nonaccredited medical schools. Dr. Abell asked whether these men from nonaccredited schools would be eligible for commissions, and Brig. Gen. Love stated that they are not eligible now.

Dr. Dukes said that in the Ninth Corps Area questionnaires have been slow coming in because of the great distances involved; also some of the younger men hesitate to sign, fearing it will put them under obligations that they do not want to assume at present. The distances involved have made a difficult problem of supplying physicians for the boards also, although the necessary number has been provided. This difficulty does not affect California as much because of the larger number of physicians available. Dr. O'Shea said that members of the Washington State Medical Society had answered the questionnaire 100 per cent and that the entire state had returned now, 93 per cent. The problem of induction boards in the northern part of the Ninth Corps Area has been difficult. The board at Missoula, Mont., had to be drawn from the breadth of the entire state. The same situation existed at Boise, Ida., where there were not sufficient specialists for the induction board. At Vancouver it was necessary to get some specialists from Portland, Aberdeen and Noquiam.

Dr. Stone reported that the induction boards had been completed in the whole Third Corps Area. With regard to the survey questionnaire, there has been much difficulty in this area in physicians not receiving the questionnaire. Great interest has been shown by hospitals and medical schools about possible disruption of their staffs by the drafting of house men. Assurance has been given that the draft officers will use discrimination so that no institution will be badly disorganized by inductions from its staff. The availability of some physicians in some communities in the Third Corps Area, as well as some health officers, came up. Dr. Osborn pointed out that the state health officers in conference with the three surgeon generals agreed that the state health officers would forward to the U. S. Public Health Service, which would forward to the surgeon generals of the army and navy, a list of health officers who it was felt were indispensable to maintain civilian health. Each state health officer has

already sent a list of indispensable employees to the U. S. Public Health Service. These lists were sent to the surgeon general of the army, who has sent copies of them to the corps area surgeons. General Love said that some of these lists apparently had been turned over to subordinates, who included in the list not only the key man but all of the men, even nurses and technicians.

Dr. Fouts of the Fourth Corps Area reported that 83.8 per cent of the survey questionnaires had been returned. Nebraska had returned 97 per cent. He supplied a list of men for the draft boards to the Adjutant General of the National Guard, Nebraska, which was submitted to the governor. Thus far he has made no recommendations for appointments on the medical advisory boards in Nebraska. He has furnished the corps area surgeon with adequate lists of specialists for service on the induction boards and at the next call in January each board will make its own arrangements with men on this list who have agreed to the call, understanding that they would not serve several days in succession but a day at a time, if possible. Dr. Fouts said that he could not provide four neuropsychiatrists for the induction boards if it requires a week or ten days of their time to go great distances away from home. There are not four neuropsychiatrists, he said, in the state of North Dakota, and how he is to get four for the board at Fort Crook is a question. An adequate panel has been turned over to the corps area surgeon for the induction boards on whom his induction board administration can call.

Colonel Spruit pointed out that it does not require four men for a board but one psychiatrist at the rate of every fifty inductants examined.

Dr. Fishbein said that in the sparsely settled states one psychiatrist would be able to give the psychiatric examinations. Circular No. 1 defined the examination simply as sufficient to rule out insanity but not the kind of examination that the average psychiatrist thinks of making when he makes an examination for legal purposes.

Dr. West said that apparently this problem in New York had been well attended to and the demands of the corps area satisfied. In New Jersey the committee has been active, but they have had some difficulties having to do with the selection of examiners for local draft boards and for advisory boards. Some governors of states have called on state committees for a list of names for consideration for appointment as medical examiners and then have paid no attention to the recommendations submitted to them but in one or two instances have put on osteopaths. Dr. Fouts said it was true in Nebraska, where they had to work over the list the third time. Colonel Spruit asked to be informed concerning unqualified men who might be appointed as examiners. Dr. West said that the request was transmitted to every state chairman and members of the Committee on Medical Preparedness. Colonel Spruit should receive all the information available about unqualified men that have been nominated to serve in these capacities by governors of states, as he is anxious to keep such men off the boards as far as it is possible to do so.

Colonel Spruit said that incompetent physicians will show up in the results of their physical examinations, as he has had occasion to observe in the first reports of examinations from some states. One man was passed who was 6 feet tall and weighed 138 pounds, and

another accepted for the draft had a perforated ear drum, both causes of rejection. Incompetent physicians on these boards can be removed if the traveling inspectors believe they are not doing a good job. The examining physicians and appeal boards are under national control, and it may be that the medical advisory boards will be placed under national control.

Dr. West said that a few men had already been commissioned in the reserves and assigned to active duty for whom the A. M. A. headquarters had no record whatever. The War Department had not asked these headquarters to check over the lists before these men had been commissioned or assigned to duty. General Love stated that they would be very glad to have a list of these names and to investigate them.

The committee asked that official lists of all physicians in selective service, and on local examining boards and medical advisory boards, and the legal member on the appeal boards be sent to the American Medical Association headquarters for checking by the Bureau of Investigation.

AFTERNOON SESSION

Report on Survey of Committee on Medical Preparedness

Dr. Leland reported on the survey being conducted by the Committee on Medical Preparedness. Since July 5, 126,489 schedules have been received. Of that number 81,853 have had the information transferred to punch cards. Of those 50,000 have been sorted in various ways for the listing of specialists, of general practitioners and of physicians in special classifications. The specialists have been listed by states for about 50,000 punch cards. Eighteen thousand general practitioners are now being listed on a specially devised form. The specialty lists are being sent to special committees that will provide the Committee on Medical Preparedness with additional information concerning residencies completed, recognized postgraduate work that the specialist has taken, and the qualifications of specialists as administrators and as teachers and research workers. Shortly, many more of these cards will be run and more names compiled on these listing sheets, giving information on additional numbers of physicians. Lists were received from some state chairmen of physicians for the Induction Boards in their areas and these were accepted at face value. Faculties of medical schools have provided the Committee with lists of teachers considered essential to the operation of the school. Many state chairmen have given much time to stimulating physicians to return their schedules. Some states have reached almost 100 per cent and others are still working diligently. Later, if a schedule from a physician over 70 years of age is not received, one will be filled out in the headquarters with the information contained in the American Medical Directory and placed in the files. Some of these men would be suitable for civilian medical care. Generally, the work in connection with the census is proceeding satisfactorily.

Questionnaires on Industrial Medicine

A special questionnaire was sent to all physicians who indicated that they were interested in devoting themselves to industrial practice. Dr. Leland thought that, when this particular survey is completed, about 6,000 industrial practicing physicians will be found.

This census will ultimately provide vast amounts of accurate and complete information which ought to be

put to some use. These headquarters are ready at all times to make the information available to those who need it.

Dr. Abell asked how many of the 126,000 replies received are from men within the active age limit. That information has not been attained yet. Dr. Fishbein, however, stated that he had figured this out for another purpose and found that there were approximately 14,000 physicians in the United States over 60 years of age. Dr. Leland stated that few of the older men refused to volunteer but that a large number of younger men will not or are undecided unless it comes to a matter of immediate war, when they would volunteer at once.

General Love stated that the work done by the various committee men will be a great help to solve the problem of supplying physicians. The idea is for them to have a year of service and then go back and have some one else take their place, unless we get into actual war and unless the physician requests an extension of service.

Dr. Crabtree said that the U. S. Public Health Service would like to have access to these data in case it needs to increase its personnel, as there may be occasion to employ other types of specialists, particularly in tuberculosis and venereal disease and possibly industrial medicine. As yet, Dr. Leland stated, lists on public health specialists or tuberculosis have not been drawn.

The committee voted to accept Dr. Leland's report and adopt it as the official record of the Committee on Medical Preparedness so far in this work.

Fee Schedule for Laboratory and Roentgen Examinations

A subcommittee of the Committee on Medical Preparedness composed of Dr. West, Dr. Fishbein and Dr. Leland previously was appointed to prepare a fee schedule for laboratory and roentgen examinations. The subcommittee obtained a schedule that had been prepared for the state of New York and sent copies to each member of the Committee on Medical Preparedness, each state chairman and the secretary of each state medical association. The committee did not approve this schedule unanimously by mail vote. The selective service system decided that it might be better to have a fee schedule for each state and instructed the state headquarters of the selective service system to confer with the medical societies about formulating schedules and that action relieved the subcommittee of the Committee on Medical Preparedness of responsibility of preparing a fee schedule to be applicable throughout the country.

Dr. West said that those schedules have been returned to him by individual men in various states with notations that some fees on the New York schedule are too high. Dr. Van Etten said that they are a little less than half of the fees provided in the workmen's compensation law in New York and that the laboratory men there were willing to make this concession as a patriotic contribution.

It was moved and voted that the schedules for laboratory and examination fees be left to the individual states and that the subcommittee of the Committee on Medical Preparedness appointed to prepare a fee schedule be discharged.

Corps Area Surgeons to Confer with Members of Committee or with State Chairman

After a discussion by various members present, it was voted that each state committeeman be responsible more or less for the affairs of his state committee through the corps area chairman of the Medical Pre-

paredness Committee and that both of them in cooperation work with the corps area surgeon to accomplish the desired ends or purposes of this committee and that all such information be communicated from one to the other.

Rejection of Registrants with Venereal Disease

General Love said that when the Committee on Medical Preparedness met, September 20, the arrangement at that time was for Wassermann tests to be taken of the registrants at the time of the induction and that all registrants with evidence of venereal lesions would be placed in a limited service class. The Surgeon General's Office considered this matter and decided that it would be better to have the blood specimens taken by the local draft boards, and since this is primarily a military training project, the army would not be warranted in taking in positive cases; that is the explanation of the reversal of policy in this matter as far as the War Department is concerned.

Colonel Spruit pointed out the advantages of having the blood specimens taken by the local boards rather than at the induction centers. Dr. Crabtree said that this procedure will provide a Wassermann dragnet that will find a great amount of syphilis and, if we take advantage of it by placing the positive cases under treatment, will advance syphilis control many years.

Dr. Fishbein said that if we could get, say by January, some statistics on the number of positive Wassermann tests in the first group and on the difficulties involved in applying serologic tests to the first group examined, it would indicate how to do it better when the large group comes along later. It may be necessary to modify some of the procedures fairly soon, and the sooner we learn what is to make these modifications necessary, the quicker the machinery can be set in motion to make the modifications. It is conceivable that by some other sudden order the whole venereal disease situation might be changed again.

It was voted that the remarks of General Love and Colonel Spruit covering this subject be made a part of the record of the Committee on Medical Preparedness.

Communities Deprived of Medical Service

Dr. Abell said that in a few locations in Kentucky and Tennessee some of the younger physicians in the Medical Reserve Corps have been ordered to active duty, leaving certain communities and hospitals deprived of men essential to carry on adequate medical service. The question of selecting men to be ordered to active duty without depriving communities of essential men was fully discussed. It was found that, as General Love stated, there had been a misunderstanding. Dr. West and Dr. Paullin pointed out that the purpose of the Committee on Medical Preparedness was to render definite help to the War Department in the selection of officers and to see that the civil communities were left with sufficient physicians to provide them with medical care. General Love stated that the corps area commanders had been directed to make a survey of reserve officers to determine those who volunteered for active service and those who could be spared from their communities, but that it was difficult for a corps area surgeon to know the requirements of the various communities in his area and to determine what men should be ordered to duty, especially if they volunteer. General Love said that we are trying to get physicians without disturbing practice in the hospitals and schools but that we have to work fast, as within the next three months about 20,000 additional hospital beds will be

opened and physicians must be had to man these military hospitals. We shall need then about 6,000 or 7,000. Dr. Fishbein stated that, if we could go before the profession with definite information about the number needed and the kind of work they need, they will be commissioned first lieutenants and paid so much, and that if their assignment to a hospital will count toward certification for an examining board it would probably be less difficult to get 5,000 physicians to volunteer. [This material appears in the current issue of *THE JOURNAL*.]

Dr. O'Shea asked whether reserve officers can still resign and General Love said that any one below the grade of captain might resign.

The motion made by Dr. Paullin that the Committee on Medical Preparedness go on record as furnishing to the Surgeon Generals of the Army, Navy and the Public Health Service a statement that the committee is willing to cooperate with them fully whether for preparedness or for war, after full discussion, was adopted.

Dr. Paullin also moved that each state committee chairman in consultation with the corps area surgeon study the members of the medical reserve corps in the various areas and, in cooperation with local or district committees, determine whether or not their services are indispensable for the community. This was discussed and adopted by the committee.

Graduates of Unapproved and Foreign Schools

Dr. Van Etten read a resolution from Kings County Medical Society, Brooklyn, which brought forth a discussion of whether men from foreign medical schools and from unapproved schools in this country should be commissioned. After discussion by various members, Dr. Fishbein pointed out that the Association, to be consistent, must support the standards of the Council on Medical Education and Hospitals, and that the Committee on Medical Preparedness could therefore only recommend that physicians who are graduates of acceptable American and Canadian schools be considered in selection for commissions. The motion was seconded and carried.

The National Youth Administration

Dr. Crabtree said that the Public Health Service had assigned to each corps area a liaison commissioned officer to expedite relations between the War Department and the public health interest of the communities; they will report for duty December 1 and in any way in which they can be of service to the Committee on Medical Preparedness or the state or local communities, they are available. The Public Health Service is already meeting the usual problems of prostitution, general health and sanitation services, medical service and hospital service in communities adjacent to army camps and industrial developments. These problems have stepped up tremendously in some of these areas, and the Public Health Service needs help.

Dr. Crabtree said that the National Youth Administration has changed its program and now is emphasizing training youth in vocations in essential defense industries. The National Youth Administration asked the Public Health Service to develop a health program for these boys under training, and a medical officer was assigned to see what could be done. In the next year it is estimated that 500,000 youths between 18 and 25 will pass under this supervision and that 60 per cent of them are indigent. This program falls into two

categories: (1) a resident project, (2) a nonresident project. In the former the youth is taken from home to some center and put in a dormitory and given vocational training and from \$6 to \$8 a month. Of these there will be some 100,000. The other 400,000 will live at home but work or go to school locally. The health program as proposed includes a physical examination and an attempt to rehabilitate the boy as far as practicable. In the resident centers they propose to employ a nurse and local physicians.

Dr. Fishbein said that the National Youth Administration is apparently attempting to carry out a medical program without telling the medical profession what it is doing. It should draw up a statement of what it is attempting. He did not think the medical profession objected to helping to take care of these boys. If the National Youth Administration would get to the profession word of what is needed, it will probably get all the cooperation it desires.

Protection of Interests of Physicians Called Into Service

Dr. West said that some communities are working on plans for looking after the interests of doctors called into active service. Dr. Dukes moved that the Committee on Medical Preparedness approve of the activities in certain states with regard to the protection of men who go to service and to approve also of what has been done to protect them legally and that the committee further study this problem and give all assistance possible to men called into service. The motion was seconded and approved.

Status of Interns and Medical Students

Dr. Abell read a letter from the Greater New York Hospital Association addressed to Col. Arthur McDermott, indicating that they had already agreed that the interns and residents in New York hospitals will, under his control, be deferred; that, he said, is what can be done in each state if one wants to by taking it up with the Selective Service headquarters in the state. Dr. Phippen said that this procedure was considered in Massachusetts, where they decided that it would be better to take each individual intern as he came up before his draft board. The Massachusetts Medical Society and the Massachusetts Hospital Association appointed a joint committee to consider such matters. Dr. West brought out that the Surgeon General had said that interns who wish to apply for commissions in the Medical Reserve Corps will be accepted if they can qualify but that they will not be assigned to active duty until they have completed their one year of internship.

Dr. Fishbein moved that the Committee on Medical Preparedness urge on all interns and residents the desirability of a year of service and that a statement be requested from the Surgeon General outlining the circumstances under which interns will be granted reserve commissions. General Love replied that such a recommendation has already been approved in the Surgeon General's Office and is now on the desk of the Chief of Staff of the Army. Furthermore, if an intern is drafted he is still eligible for a commission in the Army, but the Army ordinarily would not call him out until after he had completed his one year's internship. However, that regulation can be changed at any time. Further discussion brought out that the Navy will commission a doctor the day after graduation and give him an internship in a navy hospital. Dr. Abell said

that a number of the specialty boards appear favorable, although no definite action has been taken, to granting recognition for the year spent in that service as applied to their training. Dr. Stone said that the American Board of Surgery had agreed to that in principle with the reservation that if a man desires his service in the Army to apply to certification it would have to be of a surgical nature and not a year of general service in the Army.

Collection of Blood For Transfusion Purposes

After discussion it was moved and voted that the collection of blood for transfusion purposes be referred to a committee of the National Research Council.

Staff Personnel for New Army Hospitals

General Love said that there are to be about 70,000 hospital beds, including those now in use, and one fifth of these will be in general hospitals and the other four fifths in camp hospitals on a 4 per cent basis in each camp and varying in size from 500 beds to 2,000 beds. Between fifty and sixty doctors per thousand beds will be required. With the 20,000 beds already available in army hospitals, about 50,000 additional beds will be

provided for. The present age limit for physicians to man these army hospitals is 55 years; there is a possibility that this service may not be limited to one year but may extend to several years.

Dr. Dukes moved that the Committee on Medical Preparedness study this problem and be prepared to nominate from the various districts such men as might be required beyond draft age for the specialty groups that may be called on for the government. The motion was put to a vote and carried.

Letters

Letters were read to the committee from the Dental Preparedness Committee of the American Dental Association, from the National Medical Association and from the secretary of the New York State Medical Association, all of which were discussed. A letter was read also concerning roentgen examination of the chest of drafted men and a badge for physicians serving as examiners but not holding commissions. Dr. O'Shea moved that the subject of the badge be referred to the Executive Committee of the Committee on Medical Preparedness to report back at the next meeting. The motion was carried.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

Following is a list of additional medical reserve corps officers who up to November 25 had been ordered to extended active duty with the regular army by direction of the War Department, Washington, D. C.:

APPLEBAUM, Henry, 1st Lieut., New York.
ARMSTRONG, James Harris, 1st Lieut., Oxford, Miss.
BAGNALL, William Stanley, 1st Lieut., San Francisco.
BLOOM, Rudolph, Colonel, Philadelphia.
BOOTH, Edgar Waldo, 1st Lieut., Shreveport, La.
BROWN, Thomas Paul, 1st Lieut., Drexel Hill, Pa.
BURNSTINE, Marcus David, 1st Lieut., Columbus, Ohio.
CASEY, David Timothy, 1st Lieut., Cambridge, Mass.
CHAIN, William Thomas, 1st Lieut., Narberth, Pa.
DENHAM, Robert Hilliard, Jr., 1st Lieut., Grand Rapids, Mich.
ENGELHARDT, David Meyer, 1st Lieut., Warren, Wyo.
FANTUS, Robert Alan, 1st Lieut., Chicago.
FEIMAN, Lawrence Holt, 1st Lieut., Milwaukee.
GARDNER, Leon Philip, 1st Lieut., Aurora, Ill.
GOERINGER, Claire Ferdinand, 1st Lieut., Wilkes-Barre, Pa.
GOLD, Jacob Louis, Captain, New York.

GOLDSTEIN, Isadore Irwin, 1st Lieut., Chicago.
GRINDLAY, John Happer, 1st Lieut., Rochester, Minn.
HAINES, John Wister, 1st Lieut., Philadelphia.
HALL, Robert Milton, 1st Lieut., Denver.
JONES, Warren Candler, 1st Lieut., Sunflower, Miss.
KELLY, Delbert Cleo, 1st Lieut., Hazel Dell, Ill.
KETCHUM, Clarence Wood, 1st Lieut., Atlanta, Ga.
KOLCZUN, Michael Cornelius, 1st Lieut., New Orleans.
LARCHEZ, Albert Robert, 1st Lieut., Arlington, Mass.
LIPSON, Herbert Jacob, 1st Lieut., Grafton, N. D.
MARSHALL, James Moore, 1st Lieut., Conway, S. C.
MATHIS, Earl Nadeau, 1st Lieut., San Francisco.
McCARTHY, Alphonsus Melvin, Major, Electric Mills, Miss.
POWER, William Redmond, 1st Lieut., Merrick, L. I., N. Y.
PRIEST, Allan Eugene, 1st Lieut., Pullman, Wash.
REICHARD-ESTEVES, William, 1st Lieut., Des Moines, Iowa.
RIZZOLO, John, 1st Lieut., Newark, N. J.
SASEEN, Charles Allen, 1st Lieut., Atlantic City, N. J.
SCHOFIELD, John Thomas, Jr., 1st Lieut., Philadelphia.
SVETICH, Edward Michael, 1st Lieut., Joliet, Ill.
TALBOT, John Ralph, 1st Lieut., Marshfield, Wis.
VAN ARSDALL, Condit Brewer, Jr., 1st Lieut., Harrodsburg, Ky.

NINTH CORPS AREA

The following medical reserve officers were ordered to extended active duty by Ninth Corps Area Order for the week ended November 23. The Ninth Corps Area comprises the states of Washington, Montana, Wyoming, Oregon, Nevada, Utah, California and Idaho:

ALTOSE, Alexander R., 1st Lieut., Seattle, Fort Lewis, Wash.
BOLSTAD, Donald S., 1st Lieut., The Dalles, Ore., Fort Lewis, Wash.
COGGIN, Charles B., Captain, Los Angeles, Presidio of Monterey, Calif.
CUSTER, Clarence P., Captain, Patterson, Calif., Presidio of Monterey, Calif.

DARRAH, John R., Captain, Cody, Wyo., Fort Lewis, Wash.
GARDENIER, William H., 1st Lieut., Los Angeles, Presidio of Monterey, Calif.
HARRISON, Alexander V., 1st Lieut., Los Angeles, Fort Lewis, Wash.
KESSLER, Raymond L., Captain, Pendleton, Ore., Fort Lewis, Wash.
MINNA, John B., Major, San Diego, Calif., Presidio of Monterey, Calif.
PRESENT, Arthur J., 1st Lieut., La Jolla, Calif., Presidio of Monterey, Calif.
SCHWARTZ, Irving, Jr., Captain, San Francisco, Presidio of Monterey, Calif.
SHORT, Faulkner A., 1st Lieut., Portland, Ore., Fort Worden, Wash.
WILEY, James W., 1st Lieut., Portland, Ore., Fort Worden, Wash.

NAVAL RESERVE OFFICERS ORDERED TO ACTIVE DUTY

The following medical officers of the U. S. Naval Reserve are under orders for active duty, in addition to the names of those published in THE JOURNAL, November 16. Their rank, home address and station are indicated:

CASON, William M., Lieut. Comdr., Sandersville, Ga., Naval Air Station, Jacksonville, Fla.
CONSTANS, George M., Lieut. Comdr., Bismarck, N. D., State Director of Selective Service, North Dakota.
CRISPELL, Raymond S., Lieut. Comdr., Durham, N. C., Norfolk Naval Hospital, Portsmouth, Va.
DEYTON, John W., Lieut., Asheville, N. C., Naval Air Station, Pensacola, Fla.
GILLEN, James H., Jr., Lieut., Arlington, Va., Nav. Med. Sch., Nav. Med. Center, Washington, D. C., for instruction.

JAMESON, Edwin M., Lieut. Comdr., Saranac Lake, N. Y., Nav. Med. Sch., Nav. Med. Center, Washington, D. C., for instruction.
KENNEDY, Thomas J., Lieut. Comdr., Washington, D. C., Naval Reserve Aviation Base, Anacostia, D. C.
McCARTHY, Lawrence J., Lieut. Comdr., Boston, Naval Hospital, Chelsea, Mass.; continue duty.
RICCIARDI, Ignatius J., Lieut. (j. g.), Milwaukee, Wisconsin and Upper Peninsula of Michigan, less the Superior area.
WIESINGER, Warren E., Lieut. (j. g.), Oakland, Calif., Receiving Ship, San Francisco.
WILSON, Merton Clarke, Lieut. Comdr., Detroit, Lower Peninsula of Michigan, plus Toledo area.
WIPPERMAN, Frederic F., Lieut. (j. g.), Minneapolis, Naval Reserve Air Base, Minneapolis.
WITWER, Russell G., Lieut. (j. g.), Cleveland Heights, Ohio, Northern part of Ohio, less Toledo area.

ORGANIZATION SECTION

OFFICIAL NOTES

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

The thirty-seventh Annual Congress of the Council on Medical Education and Hospitals of the American Medical Association will be held at the Palmer House, Chicago, Feb. 17 and 18, 1941. Topics to be discussed include the place of the medical profession in the program of national defense, adjustment of medical education to social demand, coordination of professional education in medicine and allied fields, the teaching of public health and of surgery, education of Negroes, nomenclature, function of the museum in the medical school, a naturopathic subterfuge, and developments in the field of dental education. A tentative list of speakers follows:

Raymond Allen, M.D., Executive Dean, Professional Schools, University of Illinois, Chicago.

William Boyd, M.D., Professor of Pathology and Bacteriology, University of Toronto, Ontario.

C. Sidney Burwell, M.D., Dean, Harvard Medical School, Boston.

Oliver C. Carmichael, LL.D., Chancellor, Vanderbilt University, Nashville, Tenn.

Haven Emerson, M.D., formerly executive officer of the Delamar Institute of Public Health, Columbia University.

Rt. Rev. Maurice F. Griffin, LL.D., Trustee, American Hospital Association, Cleveland.

Samuel C. Harvey, M.D., Professor of Surgery, Yale University School of Medicine, New Haven.

Mr. J. W. Holloway Jr., LL.B., Acting Director, Bureau of Legal Medicine and Legislation, American Medical Association, Chicago.

Edwin P. Jordan, M.D., Assistant Editor, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Chicago.

Chauncey Leake, Ph.D., Professor of Pharmacology, University of California Medical School, San Francisco.

Edward L. Turner, M.D., President, Meharry Medical College, Nashville, Tenn.

Lewis H. Weed, M.D., Chairman, Division of Medical Sciences, National Research Council, Baltimore.

Ray Lyman Wilbur, M.D., Chairman, Council on Medical Education and Hospitals, American Medical Association, Stanford University, Calif.

The Federation of State Medical Boards of the United States will participate in the congress, covering such subjects as basic science laws, the National Board of Medical Examiners as related to medical licensure, the status of the internship, the legal status of the physician and practice violators. Among the speakers will be:

Charles Carter, Ph.D., Chairman, Iowa Board of Examiners in the Basic Sciences, Fairfield.

Mr. E. S. Elwood, Executive Secretary, National Board of Medical Examiners, Philadelphia.

Reginald Fitz, M.D., Assistant to the Dean, Harvard Medical School, Boston.

I. D. Metzger, M.D., Chairman, Pennsylvania Board of Medical Education and Licensure, Pittsburgh.

Julian F. Du Bois, M.D., Secretary and F. Manley Brist, LL.B., Attorney, Minnesota Board of Medical Examiners, St. Paul.

Dr. Ray Lyman Wilbur, President of Stanford University, will be the guest speaker at the Annual Dinner of the Federation.

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the A. M. A. meeting at Cleveland on June 3, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take

the programs at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and broadcast it at another hour or even on another day. It is advisable therefore to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme, the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in THE JOURNAL and monthly in Hygieia, the Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 11. The Family's First Friend.

December 18. A Stitch in Time.

December 25. The Country Doctor.

ADDRESSES BY OFFICIAL STAFF

DR. W. W. BAUER:

Dec. 10—University of Michigan Public Health Assembly, Ann Arbor.

Dec. 13—Will-Grundy County Medical Society, Joliet, Ill.

Dec. 16—Wells High School, Chicago.

DR. MORRIS FISHBEIN:

Dec. 12—Allegany-Garrett County Medical Society, Cumberland, Md.

Dec. 12—Cumberland Forum, Cumberland, Md.

Dec. 15—Newton Community Forum, Newtonville, Mass.

Dec. 16—Merrill Institute and Free Lecture Association, Exeter, N. H.

Dec. 17—Pharmaceutical Advertising Directors Club, New York.

Jan. 3—Academy of Medicine of Toledo and Lucas County, Toledo, Ohio.

DR. FRANK H. LAHEY:

Dec. 10-12—Southern Surgical Society, Hot Springs, Va.

Dec. 16—Fulton County Medical Society, Atlanta, Ga.

Dec. 19—Gloucester County Medical Society, Woodbury, N. J.

DR. CARL M. PETERSON:

Dec. 19—Section on Industrial Health of the Philadelphia County (Pa.) Medical Society.

DR. PAUL A. TESCHNER:

Dec. 9—Y. M. C. A., Central Branch, Chicago.

Dec. 18—Lincoln Park Kiwanis Club, Chicago.

DR. NATHAN B. VAN ETEN:

Dec. 7—Bronx Medical Association, New York.

Dec. 12—Linn County Medical Society, Cedar Rapids, Iowa.

Dec. 17—Monroe County Medical Society, Rochester, N. Y.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Personal.—Dr. Nicholas H. Dejanney, Detroit, has been appointed a member of the tuberculosis staff of the state department of health of Alabama.

Regional Meeting.—The Northwestern Division of the Medical Association of the State of Alabama met in Reform, October 10, with the following speakers: Drs. Frederick W. Wilkerson, Montgomery, "Cardiac Neuroses"; James S. Snow, Birmingham, "Drug Eruptions"; Joseph Alston Maxwell, Tuscaloosa (subject not announced); John W. Simpson, Birmingham, "The Child's Little Stomach," and David H. Wright, Berry, "Coronary Thrombosis."

CALIFORNIA

Symposium on Military Preparedness.—A symposium on military preparedness constituted the program of the Los Angeles County Medical Association at its meeting, November 7; the speakers were Judge Peirson M. Hall, selective service board; Rear Admiral David C. Cather, the navy, and Major John F. Bohlender, the army.

The Physician and the Military Emergency.—The San Francisco County Medical Society, San Francisco, devoted its meeting, November 12, to a symposium on "The Physician in Our Present Military Emergency." Dr. Philip K. Gilman, chairman of the state committee on medical preparedness, opened the meeting. Other speakers were Dr. Charles A. Dukes, Oakland, representing the selective service board; Dr. Herbert D. Crall, the army; Capt. Edward U. Reed, the navy, and Comdr. Clinton C. Defoney, the air corps.

FLORIDA

In Memory of Dr. Joseph Porter.—A housing project consisting of 136 family units will be called the Joseph Y. Porter Place to honor a physician who for many years before his death was state health officer. The project, named by the Key West Housing Authority, will be situated on recently purchased property on Trumbo Island, according to the state medical journal. Dr. Joseph Yates Porter graduated at Jefferson Medical College of Philadelphia in 1870 and in the same year was appointed assistant surgeon in the army. He was in charge of government relief measures during the yellow fever epidemic in Jacksonville in 1888 and was one of the first to support the mosquito transmission theory of yellow fever. He was appointed deputy surgeon general with the rank of lieutenant colonel and in 1907 was retired by Act of Congress. Among other positions, Dr. Porter served as quarantine inspector for the U. S. Public Health Service; president of the Florida Medical Association; for some thirty years state health officer; president of the state and provincial boards of health, 1909-1910, and camp surgeon at Camp Joseph E. Johnston during the World War. He was 79 years of age when he died, March 16, 1927.

ILLINOIS

District Meeting.—The Sangamon County Medical Society held a joint meeting with the District Medical Society of Central Illinois at St. John's Hospital in Springfield, November 7. Participating in the program were:

- Dr. Sidney O. Levinson, Chicago, Serum Transfusions or Blood Transfusions?
- Dr. Frederick A. Jostes, St. Louis, Manipulative Treatment of Backache.
- Dr. Louis H. Jorstad, St. Louis, Surgery or Radiation in Cancer of Skin and Mouth.
- Dr. Ralph H. Major, Kansas City, Mo., Changing Picture of Therapy in Pneumonia.
- Dr. Thomas D. Masters, Springfield, Chronic Peripheral Artery Disease.
- Dr. Robert J. Patton, Springfield, Endometrioma of Sigmoid with Obstruction.
- Dr. Henry S. Dickerman Jr., Springfield, The Thyroid Heart.

Chicago

Gifts to Northwestern University.—Northwestern University has received \$635,000 from the estate of the late Dr. John S. Appleman, it is reported; \$135,000 is restricted to use of the medical school clinics. Announcement has also been

made of a gift of \$162,000 from the Clara A. Abbott trust for advancement of medical, chemical and surgical science. Mrs. Abbott, widow of Dr. Wallace C. Abbott, founder of the Abbott Laboratories in North Chicago, previously had given the university \$1,500,000 for similar purposes.—A gift of \$50,000 from Miss Edith L. Patterson, Sterling, Ill., as additional endowment for the Patterson cancer clinic at Passavant Hospital, Northwestern University, was recently announced.

Society News.—The Chicago Urological Society was addressed, November 28, by Drs. Joseph H. Kiefer on "Tumors of the Testicle: Hormone Determinations in Diagnosis and Management"; Gustav Kolischer, "The Irritable Bladder," and Fay H. Squire, "Deep Roentgen Therapy in Elusive Ulcer of the Bladder: An Analysis of Twenty-Five Treated Cases."—Dr. John Alexander, Ann Arbor, addressed a joint meeting of the Chicago Tuberculosis Society and the Illinois chapter of the American College of Chest Physicians, November 18, on "Management of Bronchiectasis."—The Chicago Laryngological and Otolological Society was addressed, December 2, by Drs. Elmer W. Hagens on "Otosclerosis in Identical Twins" (case report) and Stuart C. Cullen, Iowa City, "Anesthesia in Otolaryngology."

INDIANA

State Medical Election.—Dr. Maynard A. Austin, Anderson, was chosen president-elect of the Indiana State Medical Association at its recent annual meeting in French Lick. Dr. Albert M. Mitchell, Terre Haute, will take office as president January 1. Indianapolis was selected as the place for the 1941 annual session.

Society News.—Dr. Thurman B. Rice, Indianapolis, discussed poliomyelitis before the Huntington County Medical Society, Huntington, October 2.—The Fountain-Warren County Medical Society was addressed in Kramer, October 3, by Dr. Frank W. Cregor, Indianapolis, and Mr. Thomas A. Hendricks, Indianapolis, on "United Efforts of the Medical Profession."—Dr. Russell L. Haden, Cleveland, addressed the Tippecanoe County Medical Society in Lafayette, October 8, on "Pathologic Hemorrhage and Blood Dyscrasias."—Dr. William F. King, Indianapolis, presented "Clinical Pictures of Blood Dyscrasia" before the Hendricks County Medical Society in Danville, October 24.—Lieut.-Col. Robinson Hitchcock, on the staff of the adjutant general's office, state of Indiana, discussed "National Defense and the Indiana Selective Service Plan" before the Indianapolis Medical Society, November 12. Dr. Norman E. Freeman, Philadelphia, addressed the society, November 26, on "Peripheral Circulatory Failure: Its Prevention and Treatment."

MARYLAND

Joint Psychiatric Meeting.—The Maryland Psychiatric Society and the neuropsychiatric section of the Baltimore City Medical Society will hold a joint session at Towson, December 12. Dr. Max Levin, Baltimore, will speak on "Pathogenesis of Narcolepsy" and Dr. Lawrence F. Woolley, Towson, "Technic of Curare-Metrazol Therapy."

The De Lamar Lectures.—Johns Hopkins University School of Hygiene and Public Health announced the following program for the 1940-1941 series of De Lamar Lectures:

- Dr. Virgil P. W. Sydenstricker, Augusta, Ga., November 19, Dietary Problems of the Southern United States.
- Otto A. Bessey, Ph.D., Boston, November 26, Morphological Defects in Dietary Deficiency States.
- George R. Cowgill, Ph.D., New Haven, Conn., December 3, Nutritional Deficiencies in Tropical America.
- Dr. Edward H. Hatton, Chicago, February 18, Etiology of Dental Caries.
- Dr. Max Theiler, New York, March 4, Studies on Poliomyelitis.
- Dr. Charles N. Leach, Montgomery, Ala., March 18, Recent Studies on the Epidemiology of Rabies.

MASSACHUSETTS

New Health Commissioner of Boston.—Dr. George Lynde Gately, Boston, has been appointed health commissioner of the city of Boston. He succeeds Dr. Henry F. R. Watts, who has retired on a pension after having served the city thirty-one years in different capacities. Dr. Gately graduated at Tufts College Medical School, Boston, in 1918. He is 46 years of age.

Society News.—Dr. Donald Ewen Cameron, Albany, N. Y., addressed the New England Society of Psychiatry, November 13, in Northampton on "Influence of the Times on the Teaching of Psychiatry."—Dr. Morris J. Nicholson, Boston, will speak on "Fractional Spinal Anesthesia" before the New England Society of Anesthesiology in Boston, December 10.

Dr. Albert H. Miller, Providence, R. I., addressed the society, November 12, on "Mechanics of Gas Anesthesia."—Among others, Dr. Francis S. Cheever, Boston, discussed "Observations on the Brown-Pearce Carcinoma in Roller Tile Tissue Cultures" before the Boston Society of Biologists, November 20.

MICHIGAN

Outbreak of Smallpox.—Two cases of smallpox have been reported in Detroit and 5 in Highland Park, newspapers announced November 16. These cases, the first reported in Detroit in three years, prompted Henry F. Vaughan, Dr.P.H., health commissioner, to urge all persons who have not been successfully vaccinated for smallpox within the last five years to have it done at once, it was said. There were 371 cases in the state in 1939 and 25 cases during the first eight months of 1940.

The Dr. Max Ballin Memorial Lectures.—The first lecture in the annual series sponsored by the North End Clinic, Detroit, in memory of Dr. Max Ballin was delivered, November 27, by Dr. August A. Werner, assistant professor of internal medicine, St. Louis University School of Medicine. His subject was "Recent Advances in Endocrine Therapy." The second lecture was given, December 4, by Dr. Walter C. Alvarez, Rochester, Minn., on "Recent Advances in Treatment of Food Allergy," and the last, December 11, will be by Dr. Harold J. Jeghers, Boston, assistant professor of medicine, Boston University School of Medicine, "Recent Advances in Vitamin Therapy."

NEW JERSEY

Society News.—Dr. Charles W. Mayo, Rochester, Minn., addressed the Bergen County Medical Society, Englewood, November 12, on "Surgical Treatment of Malignancy of the Right Colon."—Dr. Edward A. Strecker, Philadelphia, addressed the Camden County Medical Society, Camden, November 5, on alcoholism.—Dr. Edward Weiss, Philadelphia, addressed the Atlantic County Medical Society, Atlantic City, November 8, on "Recent Advances in Hypertension and Kidney Disease."—Dr. Tracy J. Putnam, New York, was the speaker at a joint meeting of the Academy of Medicine of Northern New Jersey and the New Jersey Neuropsychiatric Society, Newark, November 19, on "Surgical Treatment of Athetosis and Paralysis Agitans."—Dr. Waltman Walters, Rochester, Minn., addressed the Essex County Medical Society, Newark, November 14, on "Lesions of the Biliary Tract."

NEW YORK

Course on Diseases of the Chest.—The Rockland County Medical Society is presenting a course on diseases of the chest at the Summit Park Sanatorium, Pomona. The series is as follows:

- Dr. Edgar M. Medlar, Mount McGregor, Pathogenesis of Tuberculosis: Clinical Interpretation, November 15.
- Dr. William J. Ryan, Pomona, Pulmonary Tuberculosis: Early Diagnosis and Differential Diagnosis, November 22.
- Dr. Edward Percy Eglee, New York, Tuberculosis of the Lungs and Pleura; Medical and Surgical Treatment, November 29.
- Dr. Herbert C. Maier, New York, Suppurative Disease of the Lung: Suppurative Pneumonia, Abscess, Bronchiectasis, December 6.
- Dr. Francis B. Berry, New York, Benign and Malignant Neoplasms: Diagnosis, Clinical Effects and Treatment, December 13.
- Dr. Oswald R. Jones, New York, Fibrosis and Emphysema: Causes, Differentiation, Management, December 20.
- Dr. John D. Kernan, New York, Bronchoscopy in Diseases of the Chest, December 27.

The course was arranged by the committee on public health and education of the Medical Society of the State of New York.

New York City

Roentgen Examination for Drafted Men.—The tuberculosis service project of the Works Progress Administration in conjunction with the bureau of tuberculosis of the New York City Department of Health is conducting roentgen examinations of prospective selective service draftees. Mobile x-ray units are set up in four armories to make a film of each man. The films will be developed and read during the period required for the physical examinations. Most of them can be finished within one or two hours. Any men who are found to have evidence of pulmonary disease will be followed up in the routine manner by the health department's bureau of tuberculosis.

Health Preparedness Committee.—Mayor La Guardia has appointed an official Advisory Health Preparedness Committee at the request of Assemblyman Lee B. Mailler, chairman of the New York State Health Commission. The committee has twenty-three physicians, nurses and officials of private and municipal health and welfare organizations.

Among the membership are Drs. John L. Rice, health commissioner, and Willard C. Rappleye, commissioner of hospitals, representing the city; Claude W. Munger, the voluntary hospitals; George Baehr, the New York Academy of Medicine; Condit W. Cutler Jr., Harry P. Mencken, Flushing, Edward R. Cunniffe, Thomas A. McGoldrick, Brooklyn, and Arthur S. Driscoll, Staten Island, the five county medical societies. The committee is intended to function as a unit of the national defense program, operating in the public health field.

National Youth Administration to Examine Youth Employees.—A campaign of preventive medicine is being carried on among National Youth Administration youths between 18 and 24 years of age, consisting of physical tests and laboratory check-ups of the 13,000 National Youth Administration part time workers. The examinations are being conducted by the Medical Unit of the Astoria Work Experience Center, 43-02 Ditmars Boulevard, Astoria, L. I. This is the first time that medical examinations have been given youth employees by a medical unit of the National Youth Administration. In the past they have been conducted with the cooperation of various city hospitals and clinics. The examinations will cover first the youth personnel at the Astoria Center. Afterward those employed in the other centers and agencies will be brought in for tests. The medical unit is under the direction of Dr. Harold Jacobziner, assisted by seven physicians, five dentists, two dental hygienists, two nurses and a laboratory specialist. Persons showing the necessity of further treatment will be referred to the proper clinics. Frequent follow-up tests will be made by the medical unit to determine the progress in each case, and all examinations will be repeated annually. Through the cooperation of the New York City Department of Health, a portable x-ray machine will be provided for chest examinations of those young workers who show a positive reaction to the Mantoux tuberculin skin test. A vigorous campaign of health education will be carried on simultaneously with the medical program. Lectures, movies, dioramas and literature will be used. According to Dr. Jacobziner, the surveys will not show any definite results for some time. They will be carried on over a period of several years so that results may be tested and proved.

NORTH DAKOTA

"North Dakota Naturopathic Physicians, Inc."—Naturopaths must be licensed by a state board to practice in North Dakota, according to a decision handed down by Judge Daniel B. Holt, Fargo. The ruling was made in an action by the state board of medical examiners against "North Dakota Naturopathic Physicians, Inc.," a private corporation incorporated in 1938 for the stated purpose, among other things, of examining naturopaths and certifying as to their qualifications to practice in the state, according to the Grand Forks Herald. The corporation issued certificates to some of its members as "registered naturopathic physicians" and required that these certificates be filed with the register of deeds in the county in which the certificants resided, it was said. Judge Holt, in overruling a demurrer interposed by the corporation, said that, under the pleadings, the naturopaths sought to evade the laws of North Dakota and to do by indirection what they could not do directly, namely to engage in the practice of medicine without a state license. Judge H. A. Bronson, Grand Forks, represented the state board of medical examiners.

OHIO

Cleveland's Health Museum Opened.—The Cleveland Health Museum, first of its kind in the United States, was opened with a ceremony and civic luncheon November 12-13. Dr. James A. Doull, chairman of the advisory council of the museum, presided at the evening meeting. Official greetings were presented from local and national organizations and addresses were delivered by Drs. Howard Lester Taylor, president of the museum, on "From Idea to Museum in Four Years" and Bruno Gebhard, director, on "The Human Estate." Speakers at the luncheon, given by the Cleveland Chamber of Commerce were Mr. F. C. Crawford, president of the chamber of commerce, on "America's First Health Museum—Its Importance to This Community"; Mayor Harold H. Burton, "An Acknowledgement to Those Who Have Made the Museum Possible"; William J. Hutchins, LL.D., president emeritus of Berea College, Berea, Ky., "Health and National Defense," and Dr. William W. Bauer, director of the Bureau of Health Education, American Medical Association, Chicago, "Pictures of Health." The museum had its inception at a meeting of representatives of twenty-three institutions called by the Acad-

emy of Medicine of Cleveland, March 25, 1936. In December 1936 it was announced that Mrs. Francis F. Prentiss was willing to donate her former home at 8811 Euclid Avenue to the cause. During the past four years funds have been accumulated through memberships among the professions and several substantial donations. In May Dr. Gebhard, formerly curator of the Dresden Museum in Germany, was appointed director. During the summer the three story building was remodeled to provide display rooms, offices, workshops and auditorium. The opening display had 133 exhibits, most of which were made in the museum workshops.

OREGON

New Hospitals Opened.—The Blue Mountain General Hospital, a new building with a capacity of twenty beds, was opened at Prairie City in September. Dr. Oliver M. Nisbet, Portland, made an address on the progress of medicine and surgery at the opening ceremony.—A new county hospital and infirmary for Klamath County was dedicated October 13.

Medical Executives' Conference.—The fourth annual meeting of the Pacific States Medical Executives' Conference will be in Portland, December 8. Among subjects to be considered are medical military preparedness, coverage by insurance or other prepayment plans for families of low wage employee groups, the National Physicians' Committee for Extension of Medical Service, federal and state legislation and medical service plans.

Society News.—Speakers before the Multnomah County Medical Society, Portland, November 6, were Drs. Charles E. Gurney, on "Relationship of Plastic Surgery to Tumors of the Face"; William W. Baum, "Some Problems and Activities Confronting the Oregon State Medical Society"; Ralph A. Fenton, "National Problems of the Physician," and John H. Fitzgibbon, "Report of Activities of the House of Delegates of the American Medical Association."

PENNSYLVANIA

Psychiatric Meeting.—Dr. Baldwin L. Keyes, Philadelphia, was chosen president-elect of the Pennsylvania Psychiatric Society at its recent annual meeting in Philadelphia, and Dr. Henry I. Klopff, Allentown, became president. Dr. Leroy M. A. Maeder, Philadelphia, is secretary. Speakers on the program were Drs. Appleton H. Pierce, Coatesville, on "Mental Hygiene"; Samuel B. Hadden, Philadelphia, "Treatment of Neuroses by Class Technic"; Lauren H. Smith, Joseph F. Hughes and Donald W. Hastings, Philadelphia, "First Impressions of Electroshock Treatment in the Psychoses."

Philadelphia

Special Program.—The College of Physicians of Philadelphia presented a special program on medical preparedness, November 8. Francis John W. Roughton, lecturer in physiology at Cambridge University and a member of the British Committee on Blood Storage and Shock, spoke on "Blood Storage and Shock" and Lieut. Col. Arthur P. Hitchens, professor of public health and preventive medicine, University of Pennsylvania School of Medicine, discussed "A Health Program for the Home Side in War Time."

PUERTO RICO

Puerto Rico Medical Association.—The thirty-seventh annual meeting of the Puerto Rico Medical Association will be held in Santurce, December 12-15, under the presidency of Dr. Oscar G. Costa-Mandry, San Juan. Guest speakers will include:

- Dr. Louis F. Bishop, New York, Coronary Disease—Its Diagnosis and Treatment.
- Dr. Malcolm T. MacEachern, Chicago, Trends in Specialization in Medicine.
- Dr. Warren F. Draper, assistant surgeon general, U. S. Public Health Service, Washington, D. C., subject not announced.
- Mr. James A. Hamilton, director of New Haven Hospital, New Haven, Conn., Hospital Administration and the Various Methods of Securing Training.
- Dr. Arthur C. Bachmeyer, Chicago, Relations Between Hospital Administrators and Members of the Professional Staff of the Hospital.
- Mr. Rafael Picó, professor of geography, University of Puerto Rico, The White Man in the Tropics.

Puerto Rican physicians on the program include:

- Dr. Jose C. Ferrer, San Juan, Renal Pain.
- Dr. Jaime F. Pou-Valdejuili, Hato Rey, Pneumothorax in Patients of Middle Age.
- Drs. Ramon M. Suarez and Enrique Koppisch, San Juan, Weil's Disease in Puerto Rico.
- Dr. Ernesto Quintero, San Juan, Control of Venereal Diseases.
- Dr. Rafael Lopez Nussa, San Juan, Treatment of Uterine Cancer.

GENERAL

Deaths from Football Decline.—Eight deaths attributable to football occurred during the first half of this year's season, according to a report by Floyd R. Eastwood, Ph.D., Purdue University, Lafayette, Ind., record keeper for the American Football Coaches and National Collegiate Athletic associations. Five deaths resulted directly from football, two less than in 1939. Two boys died of heart disease and one from an infection. The toll has shown a downward trend since 1937, Dr. Eastwood reported.

Association for Study of Neoplastic Diseases.—The annual meeting of the American Association for the Study of Neoplastic Diseases will be held at Johns Hopkins Hospital, Baltimore, December 19-21. The meeting will consist of demonstrations of microscopic pathology and of roentgenograms and lantern slides. Session topics and chairmen will be:

- Dr. Alexander M. Duff Jr., Baltimore, Lesions of the Nasopharynx, Larynx, Trachea and Upper Respiratory Tract.
- Dr. Leopold Clarence Cohn, Baltimore, Lesions of the Breast.
- Drs. Louise D. Larimore, Greenwich, Conn., and Georgeanna Seegar Jones, Baltimore, Lesions of the Female Genital System.
- Drs. George S. Foster, Manchester, N. H., and William A. Wall, Cortland, N. Y., Lesions of the Endocrine Glands.
- Dr. Howard H. Ashbury, Baltimore, Lesions of Bone.
- Dr. Roscoe W. Teahan, Philadelphia, subject not announced.
- Drs. George A. Stewart and Sam S. Blackman Jr., Baltimore, Lesions of the Lymphoid, Myeloid and Reticulo-Endothelial Systems.

Changes in Status of Licensure.—The Colorado Board of Medical Examiners reports the following action:

- Dr. William Ewell Montgomery, Pueblo, license revoked, October 1, for conviction of a felony.

The Florida State Board of Medical Examiners reports the following action:

- Dr. Eldridge Roy Morlan, Auburndale, license revoked, June 8, for falsifying an affidavit.
- Dr. Scott Robert Edwards, now of New York, license revoked, June 8, for violation of Harrison Narcotic Law.
- Dr. Charles Russell Conway, alias Charles Wade Page, Chipley, license revoked, June 8, because of conviction of stealing an automobile and serving a sentence at the state prison at Raiford.

The Illinois State Department of Registration announces the following action:

- Dr. Archibald B. Calvin, Chicago, license restored, September 23.

The Maine Board of Registration of Medicine announces the following:

- Dr. Henry B. Esmond, Casco, license revoked, July 2, for obtaining fraudulently his license to practice medicine.

The Massachusetts Department of Registration in Medicine announces the following action taken July 11:

- Dr. Anthony Peter Carogana, Chelsea, license revoked for his conviction on charge of performing an abortion.

The South Dakota state board of health and medical examiners announces the following action:

- Dr. George E. Johnson, Gregory, license revoked, July 16, for unprofessional conduct.

Squibb Award in Endocrinology.—To promote interest in research dealing with endocrinology, E. R. Squibb & Sons have established an annual award of \$1,000 to be given through the medium of the Association for the Study of Internal Secretions, according to *Science*. The award will be given to the research worker in the United States or Canada who, in the opinion of the judges, has published during the previous calendar year the most meritorious scientific report dealing with the field of the hormones. While it will be given primarily for publication of specific papers, the judges will be given latitude in the exercise of their function. If in their judgment circumstances and justice dictate, it may be recommended that the prize be divided between two or more persons. It may also be recommended that it be made to a worker for valuable contributions over an extended period, but not necessarily representative of a given year. Membership in the association is not a requisite of eligibility for the award. A committee consisting of five members of the association will be appointed annually by the president to recommend to the council a recipient for the award. Nominations should be sent to the secretary of the association not later than January 15 for presentation at any given spring meeting. All details concerning the nominee will be considered confidential until the announcement is made at the annual dinner, when the award will be presented. While the award is intended as an annual prize, it will be withheld in accordance with the judgment of the awarding committee. In addition to the award provided by E. R. Squibb & Sons, the recipient will be presented with a simple scroll as a memento of the association, the cost to be defrayed by the association.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 9, 1940.

London Hospitals Carry on During Bombardment

The London hospitals are in the battle zone, nearer to war operations than many a field hospital in past campaigns. Many have suffered severely from bombing and one great hospital of a famous medical school has had to be evacuated, but it carries on. The history of this war will show that in Britain's heroic struggle to save herself and Europe from the new barbarism, none deserve more praise for their work and courage than the hospital staffs—medical, nursing, clerical and domestic. Exposed to bombardment day and night and sometimes even when suffering from it, they carry on not only the usual service for the sick but a well organized system for dealing with the casualties of air raids. There is an elaborate air raid precautions service with a control room and roof watchers. The latter were introduced into factories, so that after an air raid warning work could be carried on until the danger came too near. Facilities are established for carrying on in the subbasements of hospitals when the higher parts become dangerous. Here are beds to which patients in the upper floors can be removed. At nights the subbasement is a sanctuary and haven of rest for those not on duty at the time.

The medical and nursing staffs have to be on the alert every night, for then attacks from the air are much more severe than by day. The casualties are received at a special ambulance entrance and taken to a hall where they are sorted. Persons not severely injured are treated at once; the others are taken to the wards. If the upper floors have been put out of action, an emergency operating room below ground is available.

Following is an example of the courage of our hospital staffs: In southeastern England high explosive bombs cut through the kitchen quarters of a hospital, damaging wards on both sides, killing one nurse, injuring five members of the staff and causing death from shock of several elderly patients. Immediately after the bombing the nurses on duty, medical students and porters set to work to remove the patients from the damaged wards to other parts of the building. They worked while the German bombers were still overhead and splinters from antiaircraft shells were falling. The majority of the nurses were young probationers under the age of 18, who carried on with a coolness and courage to which words cannot do justice.

Casualties from Bombing of the Civilian Population

In the House of Commons Mr. Churchill stated that the Germans claimed that on the night of October 3 they dropped 251 tons of high explosives on London. On that night it took 1 ton to kill three fourths of a person. In the last war the small bombs of earlier pattern which were used killed ten persons for every ton dropped on built-up areas. Therefore the deadliness of the bomb attack on civilians in this war appears to be only one thirteenth of that in the last war. The only explanation was the vastly improved methods of shelter. When we entered this war we expected losses which might amount to 3,000 killed in a single night and 12,000 wounded night after night. We had made hospital arrangements for 250,000 casualties but up to the present as the result of air bombing we had about 8,500 killed and 13,000 wounded. Since the heavy raiding began on September 7 the figures of killed and wounded had declined steadily from over 6,000 in the first week to just under 5,000 in the second, about 4,000 in the third and under 3,000 in the last four weeks. These are casualties—dead and seriously wounded. Mr. Churchill fore-

shadowed new methods of making the wholesale bombing of the civilian population "more exciting to the enemy than it is at present," but of course he would not describe them. "It would be much better for our visitors to find them out for themselves." We must try to have as soon as possible shelters with sleeping bunks for every one in the areas liable to constant attack. Measures were being taken to secure the health of the people under these novel and primordial conditions. The official figures for the casualties in air raids during the month of September are 6,954 civilians killed and 10,615 seriously injured.

The National Health Improves Under War Conditions

In the House of Commons the Minister of Health, Mr. Malcolm MacDonald, gave a survey of the health of the nation under war conditions. He deprecated the superficial view that health services were a prime concern in peace but in war were of secondary importance, while energy was concentrated on the production of munitions. But at the machines stood hosts of men and women whose health was of crucial importance. The health of the nation was on the march and not even the calamity of war could stay it. The health statistics for 1939, in which there were eight months of uneasy peace and four months of war, were almost uniformly better than those of the preceding year, which in turn were an advance. In 1939 50 per thousand children born died before their first birthday. That was the lowest figure ever recorded and was 3 per thousand less than in 1938. It was less than half the figure for 1914, the first year of the first world war. The second significant index was the maternal mortality. This fell to 2.82 per thousand births in 1939, which was also the lowest figure ever recorded in the country and was 0.15 below the previous year and little more than two thirds of the figure for 1914. The death rate for tuberculosis did not show any decline, but the figure was encouraging. The crude death rate in 1939 from all forms of tuberculosis was 636 per million living. That was 1 per million higher than in 1938 but less than half the figure for 1914. Only one case of smallpox was notified in 1939, the figures for scarlet fever and diphtheria were lower than those of 1938, and the anticipated biennial measles epidemic failed to appear. But our health chart was not uniformly good. There was an ominous increase in the incidence of cerebrospinal fever. The disease, however, was less formidable, thanks to sulfapyridine, which had reduced the mortality by almost two thirds.

American Vans for Blood Transfusion

The Medical Research Council has received four motor vehicles equipped for medical work from the United States. They were originally purchased by the American Quakers and the International Commission for the Assistance of Child Refugees for use in France. They will now be used principally for the work of the Emergency Blood Supply depots in the neighborhood of London.

Marriages

BARCLAY MILLER BRANDMILLER, Youngstown, Ohio, to Miss Jean Elizabeth Richards in Struthers, September 19.

ROLAND SIGURD ARONSON, Philadelphia, to Miss Catherine Reimann Roess of Oil City, Pa., August 31.

EMORY HAMLIN ANDERSON, Paia, Hawaii, to Miss Janice Watkins of Oakland, Calif., August 21.

MAURICE MILTON FLIESS, Clifton Forge, Va., to Miss Irwin Rand Foster of Lynchburg, August 3.

JOSEPH NEGLEY SCHAEFFER, Dayton, Ohio, to Miss Sarah Jane Bradshaw of Bexley in August.

BEN E. EWING to Miss Mary Kline, both of Madison, Neb., June 26.

Dèaths

Oliver Thomas Osborne ☉ New Haven, Conn.; Yale University School of Medicine, 1884; member of the House of Delegates of the American Medical Association in 1902, 1903 and 1908 and member of the Council on Pharmacy and Chemistry from 1910 to 1916; vice president from 1910 to 1920, and delegate to the United States Pharmacopoeial Convention and member of the revision committee; president of the New Haven County Medical Association in 1899 and the American Therapeutic Society in 1905; fellow of the American College of Physicians; instructor of materia medica and therapeutics, 1891-1892, assistant professor of materia medica and therapeutics from 1892 to 1895, professor of materia medica and therapeutics from 1895 to 1906, professor of materia medica and therapeutics and clinical professor of medicine from 1906 to 1911, professor of therapeutics from 1911 to 1922, clinical professor of therapeutics from 1922 to 1925 and since 1925 clinical professor emeritus at his alma mater; one of the founders and chairman of the medical board of the Gaylord Farm Sanatorium, Wallingford, Conn., from 1903 to 1940; received the first Chompret Prize of the International Academy of Stomatology, in cooperation with the American Society of Stomatologists in 1933; editor of the "Section on Therapeutics" of *THE JOURNAL* from 1907 to 1919; author of "Introduction to Materia Medica and Pharmacology," 1906; co-author with Dr. Morris Fishbein of "Handbook of Therapy," 1910, ninth edition 1933; author of "Prevention and Treatment of Infections," 1915, "Disturbances of the Heart," 1916, third edition 1925, "Disturbances of the Kidneys," 1917, "Principles of Therapeutics," 1921, "What Everyone Ought to Know," 1929, "Mouth Infection," 1934, and "The Evaluation of Symptoms," 1935; section on "Acromegaly" in Buck's "Reference Handbook of the Medical Sciences," 1893, and "Organotherapy" in Cohen's "System of Physiologic Therapeutics," 1905, and more than 100 articles in medical periodicals; aged 77; died, November 11.

William Gooderham Cameron, Tacoma, Wash.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the Washington State Medical Association, American Academy of Ophthalmology and Otolaryngology and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; past president of the Pierce County Medical Society and the Puget Sound Academy of Ophthalmology; formerly member of the state legislature; at one time health officer of the village of Staples, Minn.; ophthalmologist and otolaryngologist, Northern Pacific, Tacoma General and St. Joseph's hospitals; editor of the *Bulletin of the Pierce County Medical Society*; aged 66; died, October 23, of coronary occlusion.

George Mason Magruder ☉ Senior Surgeon, United States Public Health Service, Shadwell, Va.; University of Virginia Department of Medicine, Charlottesville, 1884; was commissioned an assistant surgeon in the United States Marine Hospital, later known as the United States Public Health Service, April 24, 1886, promoted to passed assistant surgeon Aug. 4, 1890, to surgeon Aug. 5, 1899, to senior surgeon Aug. 11, 1917, and retired Aug. 13, 1927; aged 77; died, October 10, in the University of Virginia Hospital, Charlottesville, of acute myelogenous leukemia.

Robert George Cook ☉ Canandaigua, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1889; member of the American Psychiatric Association; at various times neurologist, St. Mary's Hospital, Rochester, attending neurologist, Rochester City Hospital, consulting neurologist, Rochester State Hospital, director of the Frederick Ferris Thompson Memorial Hospital; consulting physician and treasurer and formerly physician in charge of the Brigham Hall Hospital; aged 76; died, October 25, of coronary occlusion.

Paul Tonnel Dessez ☉ Medical Inspector Commander, United States Navy, retired, Waterford, Conn.; Georgetown University School of Medicine, Washington, D. C., 1897; was commissioned an assistant surgeon in the navy June 20, 1903; veteran of the Spanish-American and World wars; was retired for disability on Dec. 1, 1922; received the Distinguished Service Medal, the Navy Cross, the Croix de Guerre and the Purple Heart; fellow of the American College of Surgeons; aged 64; died, August 29.

George Michael Jennings ☉ Missoula, Mont.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1907; past president of the Medical Association of Montana and of the Montana State Board of Health; member and past president of the state board of medical examiners; fellow of the

American College of Surgeons; chief surgeon of the Northern Pacific Beneficial Association Hospital; on the staff of St. Patrick Hospital; aged 60; died, October 14.

Henry Jackson, Brookline, Mass.; Harvard Medical School, Boston, 1884; member of the Massachusetts Medical Society and the Association of American Physicians; formerly instructor in clinical medicine at his alma mater; for many years on the staff of the Boston City Hospital; aged 81; died, October 4, of coronary thrombosis.

Charles Edward Boynton Jr. ☉ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1931; on the staff of the Crawford W. Long Hospital; aged 39; died, September 25, of estivo-autumnal malaria and chronic amebiasis.

Charles Miller Glassmire, Philadelphia; Medico-Chirurgical College of Philadelphia, 1914; on the staff of the American Hospital for Diseases of the Stomach; aged 53; died, October 7, of coronary thrombosis and angina pectoris.

William T. Highberger, Maysville, W. Va.; University of Maryland School of Medicine, Baltimore, 1883; member of the West Virginia State Medical Association; aged 80; died, September 6, of hemiplegia and arteriosclerosis.

Mary Margaret Johnson, Spokane, Wash.; Cleveland Homeopathic Medical College, 1898; member of the Washington State Medical Association; aged 76; died, October 20, in Summer of cardiorenal vascular disease.

Hugo Emil Nelson, Sharon Springs, Kan.; John A. Creighton Medical College, Omaha, 1902; member of the Kansas Medical Society; aged 69; died, September 2, in the Mercy Hospital, Denver, of carcinoma of the prostate.

Newton Howard Jenkins, Kingston, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1905; aged 57; died, October 5, in the Robert Packer Hospital, Sayre, of polycystic kidney and heart disease.

Arthur Burnham Johnson, Toledo, Ohio; Rush Medical College, Chicago, 1928; for many years on the staff of the Women's and Children's Hospital; aged 43; died, October 3, of injuries received in a fall.

Cecil Norbert Brady, Newton, Mass.; Tufts College Medical School, Boston, 1913; served during the World War; aged 53; died, October 23, in the United States Naval Hospital, Chelsea, of heart disease.

Willis Sylvester Cobb, Corning, N. Y.; Albany Medical College, 1890; for many years county coroner; aged 78; died, October 5, in the Veterans Administration Facility, Bath, of coronary heart disease.

Lloyd Ephraim Strohm, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1916; aged 57; died, September 28, at Audubon, N. J., of acute cardiac dilatation and myocarditis.

Stephen Shaffer Landis ☉ Harrisburg, Pa.; University of Pittsburgh School of Medicine, 1911; for many years member of the school board; aged 53; died, October 1, of coronary occlusion.

William Edward Barton, Bethalto, Ill.; Barnes Medical College, St. Louis, 1909; formerly health officer of Wood River; aged 60; died, October 15, in Roxana of carcinoma of the stomach.

Anita Newcomb McGee, Washington, D. C.; Columbian University Medical Department, Washington, 1892; aged 76; died, October 5, of arteriosclerosis and cerebral hemorrhage.

Carl V. Cruse, Iola, Ill.; Barnes Medical College, St. Louis, 1899; member of the Illinois State Medical Society; aged 67; died, October 12, of cardiorenal disease and arteriosclerosis.

Avington Adam Edgington, Omaha; State University of Iowa College of Medicine, Iowa City, 1897; aged 75; died, October 3, of paralysis agitans and hypostatic pneumonia.

Randolph Brunson, West Orange, N. J.; Medical Department of Tulane University of Louisiana, New Orleans, 1888; aged 75; died, September 25, of cerebral hemorrhage.

James F. Gullett, Hot Springs National Park, Ark. (licensed in Arkansas in 1903); aged 76; died, October 1, in St. Joseph's Hospital of bronchopneumonia.

Elliott H. Burnett, Rockford, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1893; aged 85; died, October 1, of bronchopneumonia.

John M. Howard ☉ Amesville, Ohio; Starling Medical College, Columbus, 1895; aged 77; died, October 10, of injuries received in an automobile accident.

Hiram A. Castleberry, Ben Wheeler, Texas; University of Louisville (Ky.) Medical Department, 1895; aged 78; died, October 14, of gastric carcinoma.

Correspondence

DRUGS IN GREAT BRITAIN

To the Editor:—A note in *Science* of October 25, page 373, calls attention to the fact that important changes in medical prescribing in Great Britain are recommended by an official medical committee. Among the drugs said to be "in frequent use" and which are now hard to obtain are balsam of tolu, buchu leaves, calumba root, black catechu, gelsemium root, jalap and seneca root. Why these and many other antique galenicals and proprietary remedies are still used by British physicians is difficult to understand unless it is on the basis of steadfast British tradition. If the present war has no other good effect, it may at least serve to renovate some time worn habits in British therapeutics.

HOBART A. REIMANN, M.D., Philadelphia.

NOTE.—The *Epitome of the Pharmacopeia and National Formulary*, 1940 edition, published under the authorization of the Council on Pharmacy and Chemistry of the American Medical Association, makes the following succinct comments concerning these substances:

Balsam of Tolu. Used chiefly in the form of the syrup, which is little more than a pleasantly flavored vehicle.

Buchu. At one time largely used as a diuretic, especially in catarrhal cystitis. Value doubtful.

Calumba. Used as a simple bitter and stomachic. It appears to have no advantage over other bitters, such as gentian, except that it is free from tannin.

Gambir (Pale Catechu). Astringent; used against diarrhea in form of tincture.

Gelsemium. Used in migraine and neuralgia, and in the treatment of rheumatic, or ovarian and uterine pain. Efficacy uncertain. Untoward symptoms sometimes result from comparatively small doses.

Jalap. Drastic hydragogue cathartic, used especially in dropsies.

Seneca snake root. Employed as a nauseant expectorant (by virtue of the irritant saponin).

None of the foregoing are described in the U. S. Pharmacopeia, nor are the preparations accepted for inclusion in N. N. R.; they are not mentioned in *Useful Drugs*. They belong to those listings of drugs which are in the twilight of their existence.

The point raised by Dr. Reimann is well taken. It may be, however, that our English friends are more accustomed to the use of these drugs and therefore the lack of them may mean a hardship to those so accustomed.—En.

MEN NURSES SUGGESTED FOR AMBULANCE DUTY

To the Editor:—In THE JOURNAL November 2 under Current Comment the questionable shortage of interns is discussed, and reference is made to the amount of time that the intern has to spend on ambulance duty. It was suggested that nurses or orderlies might be assigned to the more routine ambulance duties, such as transfer of patients.

In New York City two of the public hospitals have men nurses on the psychiatric ambulances. For the record I will say that in New York State, at least, men nurses are readily available, have had sound courses of training in medical, surgical, urologic and psychiatric nursing and are duly examined by the Bureau of Nurse Examiners and licensed by the University of the State of New York.

As secretary of the Men Nurses Section of the New York State Nurses Association and chairman of the program committee of the Men Nurses Section of the American Nurses Association, I would greatly appreciate any publicity or notice which your publication would give to the use of men nurses on ambulance duty. The man nurse is physically suited to the duty, and his professional training has prepared him to accept responsibility and to use judgment. While the salary of the man nurse

is from \$105 to \$135 a month, he would release the interns for the duties which they expect.

The Men Nurses Section of the American Nurses Association has available considerable information on the national distribution of men nurses which it would gladly furnish to any employers who are seeking men nurses for this work.

NATHANIEL H. WOODING, R.N., Brooklyn.
Secretary, Men Nurses Section, New
York State Nurses Association.

TRIBUTE TO PROFESSOR WENCKEBACH

To the Editor:—With the sad announcement of the death of Prof. Karel F. Wenckebach in Vienna recently there comes to a dramatic close one of the most brilliant epochs of contemporary medicine. His passing will bring sorrow to hundreds of American physicians who enjoyed the rare privilege of basking in the warm friendship of the great group of medical scientists who made Vienna during the nineteen twenties the shrine of post-graduate teaching.

It was here at the Wenckebach Clinic that modern cardiology was born; one by one the great lights of pioneer medical thought have gone out, and all the illustrious figures who strode across the stage of the clinic platform have disappeared. Through the doors of the American Medical Association of Vienna many doctors made lasting friendships with these teachers, and all of us will recall for a long time to come the pleasant memories of this group with their special little eccentricities:

Wenckebach himself, of military mien, a little out of place, perhaps, in the gemütlich atmosphere of Vienna, stern, dogmatic but kindly and a true clinician. To him angina pectoris was not a disease entity but only a symptom and until the death of Mackenzie was the latter's chief antagonist.

Heinrich Winterberg, quiet, calm, studious, the liaison member between the clinician Wenckebach and the laboratory experts. The clinical interpreter of the science of electrocardiography and the defender of Waller, the "forgotten man" of English cardiology.

Charles F. Rothberger, hard of hearing, the technical expert of the laboratory and the originator of experimental animal research in the understanding of electrocardiography, eager, enthusiastic, a brilliant mathematician and inventor of complicated apparatus in the study of electrodynamic phenomena of the beating heart.

Jacob Pal, elder physician of the group interested in the physiology of the circulation, classifier of diseases of the arteries, inventor of the modern blood pressure apparatus, exponent of arteriosclerosis.

Rudolph Kaufmann, the American postgraduate student's personal physician, exponent of the great family doctor. A cardiologist of many specialties, brilliant diagnostician.

Theodore Meyer, pharmacologist, research worker in glyceryl trinitrate, who developed the theophylline compounds, now called aminophylline, for the relief of stenocardial symptoms, early assayer of digitalis, biochemist largely responsible for the development of the mercurial diuretics, a charming personality.

Jacob Erdheim, pathologist extraordinary, the lordly clinical ruler of the postmortem table, at whose feet sat hundreds of enthralled American students who saw dead organs alive again and the heart reliving its last episode.

Wilhelm Neumann, the thoracic clinician to whom the sounds of the heart and lungs spoke in unmistakable terms, exponent of the phonetic method of teaching and demonstrator of many physical signs in the chest.

Finally, Julius Wagner-Jauregg, dean, stern, a strict disciplinarian albeit a kindly man, perpetually astonished at the ingenuity of American excuses, sincere advocate of academic freedom for medical research, later Nobel prize winner in medi-

cine. Anticipated instinctively, perhaps, the fate of Austria and sincerely believed that the torch of scientific medicine would eventually burn brightest in the United States.

And now the school is closed; the doors are shut and the last light has gone out. All those of us privileged to have known these men will cherish the memory of the Viennese school of medical leadership which flourished from 1920 until about 1928, and to every one who knew him the passing of the chief himself, Wenckebach, must call forth wistful thoughts of a medical era now definitely gone.

ALBERT S. HYMAN, M.D., New York.

President, Alumni Society of the American
Medical Association of Vienna.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

NICOTINIC ACID FOR TOXIC MANIFESTATIONS OF SULFANILAMIDE

To the Editor:—In *The Journal* for March 2, 1940, page 756, Dr. Doughty reported the successful treatment of certain toxic manifestations of sulfanilamide with nicotinic acid. A pharmaceutical house has asked if there is sufficient evidence to warrant the inclusion of nicotinic acid in a tablet of sulfanilamide. As this is not mentioned in the recent paper by Dr. Long, I am wondering whether such a combination would be justifiable?

M.D., Canada.

ANSWER.—The available data concerning the use of nicotinic acid in preventing the toxic manifestations which may arise in the course of sulfonamide therapy are contradictory. Certain observers have reported that large doses of nicotinic acid (from 200 to 400 mg. a day) will decrease nausea and vomiting, cyanosis and other toxic manifestations of sulfanilamide therapy. Since McGinty's original report on this subject (McGinty, A. P.; Lewis, G. T., and Holtzclaw, M. R.: *J. M. A. Georgia* 28:54 [Feb.] 1939), an attempt has been made in the Johns Hopkins Hospital to evaluate nicotinic acid in the prevention of the toxic manifestations which arise in the course of therapy with sulfanilamide and its derivatives. In certain cases it has seemed that the administration of nicotinic acid decreased nausea and vomiting, cyanosis, and the like, while in other cases treatment with nicotinic acid has had absolutely no effect on the toxic reactions of sulfanilamide. Because completely satisfactory methods of evaluating nicotinic acid deficiency states in human beings are not available, it has been impossible to determine whether the apparent good results from combined therapy in certain cases resulted from the abolishment of a deficiency state. At the present time the proposed combination of nicotinic acid with sulfanilamide in tablet form would not appear to be based on sound clinical observations.

HYPOGONADISM IN BOY

To the Editor:—What is the present treatment of hypogonadism in a youth 17 years old who is in perfect health and mentally alert and who shows absolutely no evidence of secondary sex characteristics? Will you please discuss the probability of improvement and the likelihood of permanence of results?

L. C. Howe, M.D., Muscatine, Iowa.

ANSWER.—It is assumed that gross pituitary disease has been ruled out as far as possible by x-ray examinations of the skull and visual fields. This step is necessary whether the patient has suggestive complaints or not. The essential defect may lie in the pituitary body or in the testes. Large amounts of follicle stimulating material may be found in the urine if the defect is gonadal, but the techniques for its best measurement are as yet not agreed on and are not available for those without the services of a research laboratory. The results of treatment may answer this question. Pregnancy urine extract 500 international units three times weekly may be administered for a period of from four to six months, the results judged by a photographic record of progress. This dose should be achieved by graded steps and may even be doubled if well tolerated. If the response is satisfactory, treatment should be continued; if none is secured, the

testes must be regarded as refractory and androgens used. Testosterone propionate 25 mg. intramuscularly three times weekly will usually produce unmistakable results in from three to four months or less. Androgenic and gonadotropic therapy are substitutional and regression of sex development may be expected if the patient is eunuchoid or suffers from pituitary dysfunction. This may be a case of delayed puberty in which the prognosis for normal sexual development is good.

FORMALDEHYDE POISONING

To the Editor:—I should like to know the possible symptoms and signs found in people working with formaldehyde. A patient complains of weakness, dizziness and tingling of the fingers and nervousness and loss of weight. Physical examination gives negative results. Urinalysis is negative. The electrocardiogram is essentially normal. Blood examination reveals erythrocytes 4,710,000, hemoglobin 14 Gm., color index 0.96, leukocytes 8,800. The differential count is essentially normal.

Earl Herron, M.D., Chicago.

ANSWER.—The characteristic manifestations of industrial formaldehyde poisoning are conjunctivitis, coryza, bronchitis, dermatitis, increased sensitivity of the skin in the absence of dermatitis, dizziness and feeling of great weakness. These symptoms appear in mild acute cases resulting from inhalation of the formaldehyde gas and in the case of cutaneous lesions direct contact with formaldehyde in solution. More prolonged involvement intensifies these lesions and in addition there may appear the symptoms of kidney irritation such as anuria, softened, necrotic fingernails, gastro-enteritis, rarely bronchopneumonia, hepatitis, anorexia, sleeplessness and palpitation.

The symptoms mentioned are compatible with the diagnosis of formaldehyde injury, but one could expect concomitant signs of irritation of the eyes, the upper and lower respiratory tract or the skin.

NAUSEA AND VOMITING FROM GENTIAN VIOLET PILLS

To the Editor:—I am treating a family infected with pinworms—*Oxyuris vermicularis*—with gentian violet pills, according to the routine described in *The Journal*, June 8, 1940. I find nausea and vomiting so severe that carrying out the routine is impossible. Is there a way of overcoming this?

M.D., Connecticut.

ANSWER.—Nausea and vomiting and even diarrhea may occur during the oral administration of gentian violet. These symptoms quickly subside on withdrawal of the drug.

The use of a coated tablet that does not disintegrate in the stomach is advised since not only is less gastrointestinal irritation produced but the effectiveness against oxyuriasis is enhanced. The diet should contain a moderate amount of roughage, fatty foods should be avoided and alcohol should be interdicted. It may be necessary to reduce the dosage or even to stop the drug for from twenty-four to forty-eight hours and continue the treatment with the maximum dose that is tolerated without unpleasant symptoms. In these instances it is recommended that the period of treatment be extended so that the total calculated dose is taken. Small doses of bismuth subnitrate may aid in allaying gastrointestinal symptoms.

PROPHYLACTIC VACCINATION FOR UNDULANT FEVER

To the Editor:—There have been a number of scattered cases of abortus fever among cows in this region; there have also been occasional cases of human infection. Veterinary men "vaccinate" cows against this. The situation is better now. We medical men use the vaccine for therapeutic purposes when needful. I have seen no reports in *The Journal* of the use of vaccine for prophylactic purposes and write to inquire: In the presence of an endemic or partial epidemic situation, when individuals have used milk from infected cows without pasteurization (and without boiling) what doses of the vaccine should be given? How long does it take for immunity to be thus established? How often or at what intervals should the doses be given and should such doses be graduated upward progressively? Is it possible to obtain immunity by any means before the end of the incubation period of the trouble is reached in man? Are there any antitoxins known or on the market? If a family has been continuously using the milk from a cow now suspected to have had the trouble for one and one-half years past have they probably not developed a certain amount of immunity? Can an intensive short course of vaccination be put in operation by using short intervals between injections? I have used with success the combination of sulfanilamide and vaccine.

Matthew Karasek, M.D., Shidler, Okla.

ANSWER.—Prophylactic vaccination of human beings against *Brucella* infection has not been studied on a scale sufficient to demonstrate its value. The fact that serum agglutinins may appear in relatively high titer following a cutaneous test with diluted *Brucella* vaccine or brucellergin in presumably normal individuals points to the possibility that protection might be afforded by vaccination. There is need for controlled studies in this field.

QUERIES AND MINOR NOTES

Jour. A. M. A.
Dec. 7, 1940

POLYNEURITIS OF PREGNANCY

To the Editor:—Is there evidence to show that parenteral administration of thiamine or liver extract would be more effective than oral administration? What would be considered effective treatment for a case of polyneuritis of pregnancy? How long should intensive vitamin therapy be continued before abandoning it as ineffective? The patient in question is a well nourished woman with myopia. The stated age is 36, the apparent age 50 years. There have been grand mal seizures since chorea at about 11 years. They have been controlled the past three years with phenobarbital 0.1 Gm. daily. She is a septipara, entirely normal except for the last recent gestation, which began with severe vomiting, dyspnea on slight exertion and irregular pulse. Although I feared for her life, she easily delivered a 9 pound (4,000 Gm.) infant, after which a moderate edema rapidly cleared away. For the past two years she has had rather severe left sciatic neuritis, in the hope of curing which all teeth were futilely removed. After delivery this pain was still annoying her but in addition she complained of numbness and tingling of both legs, more on the left. The proprioceptive sense in the feet and toes has decreased but is not gone. The knee jerks were exaggerated about the tenth postpartum day but now two months later they are only faintly active. Now (two months post partum) Romberg's sign is negative. The finger to nose test is normal on both sides. There is staggering gait, which is seemingly due to weakness. She turns her ankles frequently. The pupils react sluggishly to light. Her tongue is covered with short fur, is smooth on the edges and has been subject to soreness several times in the past two months. Two weeks after delivery free hydrochloric acid was present in the stomach produced by alcohol stimulation but is produced by histamine injection, to which she had a severe general reaction. The red blood count is 4,700,000, the hemoglobin 104 per cent, Sahli. The spinal fluid is normal and under low pressure. The Kahn reaction is negative. She has been taking about 2.25 Gm. of dried brewer's yeast daily for six or eight weeks but no distinct improvement has occurred. She has had a small amount of liver. Phenobarbital was discontinued for a month for fear it might have been a contributing factor, but because of recurrence of epileptic seizures it has been resumed.

ANSWER.—There is considerable clinical and experimental evidence to show that parenteral administration of either thiamine hydrochloride or liver extract is far superior to that of oral administration. The oral administration carries with it a questionable amount of absorption. In a 3,600 bed charitable hospital vitamin B₁ and liver are given parenterally. The following is suggested as an effective therapy for a case of polyneuritis of pregnancy: 3,000 units of vitamin B₁ or thiamine hydrochloride or vitamin B complex daily hypodermically for a period of from twenty-one to thirty days; a diet rich in vitamin B content such as yeast, liver, whole wheat bread, cereals, eggs, nuts, lean pork, milk, vegetables and rice polishes; nicotinic acid (vitamin B₂) in doses of 50 mg. ten times a day for three weeks and possibly for four before concluding that it is ineffective. From the evidence submitted in this case one should be suspicious of a subacute combined degeneration of the spinal cord related to either avitaminosis or pernicious anemia.

Theodore E. Wade, M.D., Pueblo, Colo.

NO ARTERIES EXEMPT FROM ATHEROSCLEROSIS

To the Editor:—Do you know of any artery or groups of arteries in which intimal thickening, atherosclerosis or medial sclerosis never develops? In other words, are there any arteries in the body in which the lumen always remains of the same caliber and the walls remain free of destructive processes throughout life?

ANSWER.—There is no artery which is always free from pathologic changes during a long life, although occasionally essentially normal coronary arteries are found in persons 60 years of age. Cerebral arteries are usually attacked late in life. Paradoxically the main renal arteries show less atherosclerosis than the other abdominal branches of the aorta. Lesions extending from the orifices for a short distance are common. Great hypertrophy of the media may occur with hypertension, but up to the division of the vessel there is frequently no atherosclerosis.

Roy J. Popkin, M.D., Los Angeles.

SOAP SUBSTITUTES FOR SENSITIVE SKIN

To the Editor:—A patient develops an allergic response to every form of soap used. Can you suggest to me some substitute for soap?

ANSWER.—Sensitivity of the skin to soap may be either non-specific or specific. Nonspecific dermatitis is due to the lack of tolerance to the alkali content of most soaps. It is characteristic of highly irritable skin that its tolerance for alkali is low. For this reason most dermatologists forbid the use of soap (everywhere except on the scalp) in cases of eczema. Specific sensitivity to soap may be due to dyes, perfumes and other extraneous ingredients, rather than the salts of the fatty acids, which are the components of soaps. Among the ingredients to which specific sensitivity is to be considered are cottonseed oil and flaxseed oil in persons sensitive to these substances.

Milton H. Erickson, M.D., Eloise, Mich.

Soap substitutes that are frequently used are oils, as liquid petrolatum, sesame oil and various vegetable oils. Each of these should be tried in turn for the patient's tolerance to it. Another group of substances used as soap substitutes are the various sulfonated oils available commercially. They have a drying effect on the skin and may require the use of a small amount of oil afterward to counteract this effect. It should be determined that the oil used is nonirritating to the individual patient.

SYPHILIS OF MOTHER, NURSING AND CONTINUED TREATMENT

To the Editor:—A woman in the fourth month of pregnancy is discovered to have positive tests for syphilis. No signs or symptoms of activity are present and the date of infection is unknown. Intensive continuous treatment was carried out to the time of delivery of a full term normal baby. The mother's tests have been persistently positive. Assuming for the sake of argument that her disease is truly latent, that her treatment was adequate by all standards and that the baby is nonsyphilitic, (1) May the mother nurse the baby? (2) May the mother have a postpartum rest period or a rest at any time during nursing?

ANSWER.—1. The mother may nurse the baby. 2. For her own sake the mother would require more treatment than one supposes her to have had on the basis of the information supplied, and treatment therefore should be continued. If, however, she has been adequately treated for her own sake, further treatment is not necessary simply because she is nursing the baby.

M.D., Illinois.

POLYCYTHAEMIA VERA

To the Editor:—I am a victim of polycythaemia vera. Please inform me regarding the technic that I should use on myself with a simplex Westinghouse x-ray machine of 50 milliamperes and 85 kilowatts in treatment for this condition. If my blood count is 7,000,000, just what technic should I use.

ANSWER.—Most internists and hematologists agree that polycythaemia vera is best treated by venesection. Irradiation may be tried. One hundred roentgens is given over the spleen three times a week for two weeks. Further irradiation must depend on the blood count.

M.D., Idaho.

FREQUENT MENSTRUATION AND ENLARGED THYROID IN YOUNG GIRL

To the Editor:—A girl aged 15 menstruates every two to three weeks and has a noticeable enlargement of the thyroid. She is entirely normal otherwise. In seeking authoritative opinions I have received conflicting advice. On the one hand it was suggested that she be given antithyroid-5 and that the administration of thyroid in adolescent goiter is often of aid with increased thyroid activity and the frequent menstrual periods is contraindication to any type of estrogenic therapy, the preparation of choice being corpus luteum.

ANSWER.—There is no connection between the enlargement of the thyroid and the frequent menstruation. The only treatment indicated in such cases is a small dose of iodine (about 10 mg. of potassium iodide a week) to prevent further enlargement of her thyroid. No attempt should be made to influence ovarian function at this age, because some spontaneous adjustment may occur soon. Moreover, the frequency of menstruation shows a considerable amount of normal variation.

M.D., Wisconsin

TYPHUS VACCINES

To the Editor:—In Queries and Minor Notes (The Journal, Oct. 5, 1940, p. 1218) in answer to an inquiry about typhus vaccines and serums it was stated that up to the present time typhus vaccines are still in the experimental stage. Two vaccines seem to have outgrown the experimental stage and are successfully employed in routine vaccinations: 1. Weigl vaccine (Professor Weigl, director of the Polish Institute at Lodz) is considered the most effective vaccine made from the intestine of lice which have been infected with *Rickettsia prowazekii*. 2. The Weigl vaccine (Dr. Rudolf Weigl, author of the chapter on the typhus fever group, Handbook of Virus Diseases, 1939, vol. 2, p. 528; Arb. Inst. 122: 220, 1939) does not use the classic *Rickettsia prowazekii* but Rickettsia mooseri, the virus of the murine typhus, and Weigl prefers Cox's method (chicken embryo, vitelline sac inoculation, Pub. Health Rep. 53: 2241 [Dec. 23] 1938). Weigl was making vaccine on a larger scale for the Polish campaign of the German army last fall and winter. Statistical data relating thereto could not yet be obtained. Latest reports refer to the discovery of a specific toxin, probably an endotoxin (Gildemeister and Haagen). This *Rickettsia* toxin is not more resistant than the virus itself and can be destroyed by formaldehyde, heating to 60 C. or storage for seven days. In mouse experiments typhus serums neutralized the specific toxin and thus prevented the occurrence of the typical exanthem as well as circulatory and nervous symptoms while they prevented incubation of infection only in single cases.

F. O. W. Voigt, M.D., Oskaloosa, Iowa.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, November 30, page 1910.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 17-19. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, Jan. 7. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

CALIFORNIA: Oral examination (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, Dec. 11. Written. Los Angeles, Feb. 24-27. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

COLORADO: * Denver, Jan. 7-10. Applications must be on file not later than Dec. 23. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

DELAWARE: July 8-10. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

GEORGIA: Atlanta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 8-11. Sec., Dr. James A. Morgan, 48 Young Building, Honolulu.

IDAH0: Boise, April 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 335 State Capitol Bldg., Boise.

ILLINOIS: Written. Chicago, Jan. 21-22. Reciprocity. Chicago, Jan. 23. Supt. of Registration, Dept. of Registration and Education, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 17-19. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, Citizens Trust Bldg., Fort Wayne.

IOWA: Des Moines, Dec. 9-11. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

MARYLAND: Regular. Baltimore, Dec. 10-13. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. Homoeopathic. Baltimore, Dec. 10-11. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: * Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: * Minneapolis, Jan. 21-23. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: Reciprocity. Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: Reciprocity. Helena, March 31. Written. Helena, April 1. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: Reciprocity with oral examination, Feb. 3. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: Concord, March 13-14. Sec., Board of Registration in Medicine, Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, June 17-18. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 14-15. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 27-30. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, State Education Department, 315 Education Bldg., Albany.

NORTH CAROLINA: Reciprocity. Durham, Dec. 10. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Sec., Dr. G. M. Williamson, 413 S. Third St., Grand Forks.

OHIO: Columbus, Dec. 9-12. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * Oklahoma City, Dec. 11. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: * Portland, Jan. 14-16. Exec. Sec., Miss Lorienne M. Conlee, 603 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia, January 7-11. Acting Sec., Bureau of Professional Licensing, Miss Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, Jan. 2-3. Sec., Division of Examiners, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH DAKOTA: * Pierre, Jan. 21-22. Dir., Medical Licensure, Dr. J. E. D. Cook, Pierre.

TENNESSEE: Memphis, Dec. 18-19. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

WASHINGTON: Seattle, Jan. 13-15. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WISCONSIN: * Madison, Jan. 14-16. Applications must be on file not later than Jan. 2. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, Feb. 3-4. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, Dec. 17. Sec., Dr. Robert L. Nugent, University of Arizona, Science Hall, Tucson.

COLORADO: Denver, Dec. 9-10. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

CONNECTICUT: Feb. 8. Address State Board of Healing Arts, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, April 21-22. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

IOWA: Des Moines, Jan. 14. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor, Detroit and East Lansing, Feb. 14-15. Sec., Miss Flora E. Dube, East Lansing.

MINNESOTA: Minneapolis, Jan. 7-8. Sec., Dr. J. Charnley McKinley, University of Minnesota, 126 Millard Hall, Minneapolis.

NEBRASKA: Omaha, Jan. 14-15. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, Feb. 15. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

SOUTH DAKOTA: Endorsement. Yankton, Dec. 21. Sec., Dr. Gregg M. Evans, Yankton.

WASHINGTON: Seattle, Jan. 9-10. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

Idaho April Report

Mr. H. B. Whittlesey, director, Bureau of Occupational Licenses, reports the written examination for medical licensure held at Boise, April 2-6, 1940. The examination covered twenty-one subjects and included 140 questions. An average of 75 per cent was required to pass. Twenty-three candidates were examined, twenty-two of whom passed and one failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1937)	79,	81.5
Loyola University School of Medicine.....	(1940)	85	
Northwestern University Medical School.....	(1928)	81,	
(1936) 79, 83, (1938) 82.5, (1939) 79, 83			
Rush Medical College.....	(1937)	83.5,	
(1938) 82, (1939) 81.5			
University of Illinois College of Medicine.....	(1935)	81	
University of Louisville School of Medicine.....	(1939)	83	
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1935)	83,	
University of Michigan.....		79	
Washington University.....	(1939) 81.5	83,	
Creighton University School of Medicine....	(1933)	83	
University of Oklahoma School of Medicine.....	(1939)	83	
University of Oregon Medical School.....	(1932) 81, (1939)	82.5	

School	FAILED	Year Grad.	Number Failed
Regia Università degli Studi di Bologna. Facoltà di Medicina e Chirurgia.....	(1937)		1

Pennsylvania Reciprocity Report

Miss Marguerite G. Steiner, acting secretary, Bureau of Professional Licensing, reports thirty-three physicians licensed to practice medicine by reciprocity and twenty-one physicians so licensed by endorsement from January 26 through September 18. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine.....	(1931)		Colorado
Yale University School of Medicine.....	(1932)		Connecticut
Loyola University School of Medicine.....	(1938)		Illinois
Rush Medical College.....	(1931), (1937)		Illinois
(1934) Michigan			
State University of Iowa College of Medicine.....	(1935)		Iowa
Johns Hopkins University School of Medicine.....	(1933), (1937)		Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1936)		Maryland
Harvard Medical School.....	(1939)		Maryland
University of Michigan Medical School.....	(1929)		Michigan
Wayne University College of Medicine.....	(1940)		Michigan
University of Minnesota Medical School.....	(1936)		Minnesota
St. Louis University School of Medicine.....	(1935)		Florida
University of Nebraska College of Medicine.....	(1933)		Nebraska
Columbia University College of Physicians and Surgeons.....	(1932), (1934, 2)		New York
Cornell University Medical College.....	(1924)		New York
Long Island College of Medicine.....	(1935)		New York
University of Buffalo School of Medicine.....	(1932)		New York
Ohio State University College of Medicine.....	(1933)		Ohio
University of Cincinnati College of Medicine.....	(1927)		Ohio
Hahnemann Medical College and Hospital of Philadelphia.....	(1934), (1935)		New Jersey
Jefferson Medical College of Philadelphia.....	(1929)		Texas
(1935) West Virginia			
Temple University School of Medicine.....	(1937)		Kentucky
University of Pennsylvania School of Medicine.....	(1928), (1934)		New Jersey
McHarr Medical College.....	(1937)		Tennessee
University of Tennessee College of Medicine.....	(1930)		Tennessee

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad.	of
Georgetown University School of Medicine.....	(1938) N. B. M. Ex.		
Northwestern University Medical School.....	(1938), (1939) N. B. M. Ex.		
Johns Hopkins University School of Medicine.....	(1938), (1939) N. B. M. Ex.		
Boston University School of Medicine.....	(1938, 2) N. B. M. Ex.		
Harvard Medical School.....	(1925), (1932), (1934), (1936), (1937) N. B. M. Ex.		
Washington University School of Medicine.....	(1934) N. B. M. Ex.		
Columbia University College of Physicians and Surgeons.....	(1932) N. B. M. Ex.		
Syracuse University College of Medicine.....	(1938) N. B. M. Ex.		
Duke University School of Medicine.....	(1937, 2), (1939) N. B. M. Ex.		
University of Cincinnati College of Medicine.....	(1929) N. B. M. Ex.		
University of Pennsylvania School of Medicine.....	(1935) N. B. M. Ex.		
Woman's Medical College of Pennsylvania.....	(1938) N. B. M. Ex.		

Book Notices

The Emperor's Itch: The Legend Concerning Napoleon's Affliction with Scabies. By Reuben Friedman, M.D., Assistant Professor of Dermatology and Syphilology, Temple University School of Medicine, Philadelphia. Cloth. Price, \$1.50. Pp. 82, with 10 illustrations. New York: Froben Press, 1940.

It is said that 40,000 books have been written on the life of Napoleon, but the present interesting monograph by Friedman is the first which discusses an annoying disease of the skin from which he suffered for many years. This phase of Napoleon's life has either been overlooked or been misunderstood by previous biographers.

The story that the disease of the skin from which Napoleon suffered was scabies is shown by the author to be a myth. There are no authentic records to prove that he ever had this disease. In view of the emperor's cleanly habits and the long duration of the disorder and because of the numerous sulfur baths which he took, it seems impossible that the disease could have been scabies. Furthermore, the Empress Josephine is not known to have suffered from scabies, although Napoleon's second wife, Marie Louise, is said to have been affected. However, it has been stated that she was somewhat promiscuous sexually. Finally, the remedy which his physician Corvisart used successfully was an extremely weak and practically useless one for the treatment of scabies.

The author suggests with good reason that Napoleon actually suffered from dermatitis herpetiformis, which began with the siege of Toulon and lasted for nine or ten years. The temporary "cure" effected by his physician coincided with the period of his life when he was able to rest and be relieved of the strain of his military campaigns. The author also thinks that Napoleon's characteristic pose with his hand beneath his shirt was a mannerism possibly cultivated in his boyhood. He does not think it was due to itching from his cutaneous disease.

This book is a most readable one and contains many references and interesting illustrations.

An Introduction to Medical Genetics. By J. A. Fraser Roberts, M.A., M.B., D.Sc., Principal Investigator to the Burden Mental Research Trust, Stoke Park Colony, Stapleton, Bristol. Cloth. Price, \$4.50. Pp. 266, with 94 illustrations. New York & London: Oxford University Press, 1940.

Works on human heredity have not heretofore been distinguished by any evident relevance for clinical medicine. In Dr. Roberts's volume, perhaps for the first time, the relation of genetics to medical practice, and especially to medical research, can be seen clearly. The author, moreover, by a somewhat novel method of presenting genetic principles has achieved a clarity and simplicity which are exceptional, in comparison not only with other textbooks but even with avowed popularizations of the subject.

There is no conventional prefatory section on genetic principles. Instead there is a discussion in turn of each type of mating which may be encountered in man: normal by abnormal, abnormal by abnormal and normal by normal, for conditions which exhibit respectively dominant, recessive or incompletely dominant inheritance, and autosomal or sex linked transmission. The discussion of each case is in terms of a familiar human abnormality and is followed by a clear explanation of the chromosomal basis for the observed results. Genetic principles, developed gradually in the course of the book, are limited strictly to those which are immediately applicable to human material. Special statistical methods, necessary for the actual analysis of human hereditary mechanisms but not essential for an understanding of them, are not elaborated, but the precautions which must be observed in the collection and interpretation of data in order to avoid the commoner statistical fallacies are carefully pointed out. Even so difficult a subject as the detection of human linkage is not ignored, and once again the author explodes the still current notion that the association of two abnormal traits indicates that they are linked in the genetic sense.

Topics of subsidiary importance or of especial technical complexity are relegated to fine type and may be omitted by the reader without sacrificing the continuity or coherence of the

remainder of the text. But in spite of the modest dimensions of the book it is doubtful whether any single principle essential for the understanding of human genetic methods fails to receive at least passing attention, with judicious orientation into what is already an unwieldy literature for the uninitiated.

There are inevitably some sections with which it would be tempting to take issue. Thus Roberts seems overoptimistic with regard to the prognostic possibilities promised by the prospect of constructing linkage maps for man. It is quite true, of course, that the accumulation of cases of genetic linkage is almost bound to follow any systematic effort to discover them. But it is a far cry from the discovery of isolated cases of linkage to the development of usable gene maps such as have been elaborated so brilliantly for *Drosophila* and maize. Even in the mouse, in which the difficulty inherent in a larger number of chromosomes is roughly of the same magnitude as in man, chromosome maps are still a dream for the future in spite of this animal's convenience for laboratory experiments and the extensive genetic investigations of which it has been the subject. This is not to deny the value of linkage studies in man but it does suggest the importance of pursuing human genetic studies as human genetics and of recognizing at the outset the conditions (not all unfavorable, as is frequently supposed) which establish the methodology of human heredity on a somewhat different level from that of the genetics of laboratory bred animals.

It is the special merit of the book that it reveals the conditions by which human genetics, especially in its medical aspects, is qualitatively distinguished from the conventional genetics of the animal or plant breeder. And it is important to recognize that the classic materials presented in standard biologic textbooks may give a misleading or totally false picture of what is to be expected in human material. The excellent sections on the similar effects of different genes, on the variable expression of heredity factors and on heredity as a factor in the causation of disease, together with constant emphasis on the peculiar significance of gene frequency in man, succeed in establishing the proper orientation. One gets the impression that the part played by heredity in a large majority of pathologic conditions is to determine the presence or absence of a constitutional peculiarity which might be called a diathesis, although it involves a more tangibly determinable condition than that term usually connotes. From the evidence available it seems almost certain that this situation is far commoner than is any unequivocal one to one correspondence between gene and disease. Genetic study can assist the clinician by making possible the detection of diathetic individuals even when they do not develop the disease, and this should facilitate the detection of such controllable nongenetic factors as infection, diet and mechanical irritation, which may play a part in transforming an inherited diathesis into a patent pathologic condition.

The reader should be warned that Dr. Roberts's theoretical discussions of the various ways in which genetic factors may be concerned in the development of disease have the appearance of being rather more speculative than need be. This is partly to be attributed to a commendably conservative approach but chiefly, perhaps, to the author's limiting himself exclusively to human heredity in his choice of illustrative material. In this connection primarily the disadvantages of this restriction are seen, for a judicious selection of well established analogues from animal genetics would have furnished a firmer basis for many of the inferences which appear rather tenuous when supported only by observations from the less adequately studied human material. For example, the author suggests that certain genes may act by rendering the developing embryo especially sensitive to environmental variations which are without effect on genetically normal organisms; the suggestion would appear less gratuitous if it were indicated that this type of action has frequently been demonstrated for genetic factors studied in laboratory animals. And the whole field of what is commonly called developmental or physiological genetics has such an intimate bearing on the specifically medical problems of human heredity that some familiarity with its methods and results would seem to be an indispensable part of the medical geneticist's background.

The defects which may be found in this volume are minor in comparison with the values inherent in its fresh outlook and in its temperate treatment of most problems. Of specific sections, the chapter on multifactor inheritance is perhaps the least satisfactory, and it would probably have been better to omit entirely a consideration of hereditary factors in intelligence if it was not possible to give somewhat more extensive indication of the complexities of the problem. The practical minded reader may be disturbed by the fact that many of the illustrations of clearcut mendelizing pathologic conditions are still such rare or insignificant aberrations as albinism, alkaptonuria or polydactyly. But an understanding of the book will involve recognition that this is largely a consequence of the inadequacy of traditional methods in human genetic research and an appreciation of the fact that the importance of genetics for medicine considerably transcends its relevance to such conditions as those just enumerated. The use of genetic methods as a tool to supplement the usual methods of clinical research is more than likely to shed light on the etiology and pathogenesis of leukemia, gastric ulcer and essential hypertension, for example, and to prove profitable in the further study of such infectious diseases as rheumatic fever and poliomyelitis, to name only a few of the conditions in which there is already some basis for inferring the importance of hereditary factors.

Medical practitioners and investigators will find the book a comprehensible and stimulating guide to the applicability of genetics to medicine. It can also be recommended to specialists in animal or plant genetics who wish a clearer idea of some of the human applications of their subject. And it should prove an admirable textbook either for a semester's course in the premedical curriculum or as the basis for a brief lecture series in genetics for medical students.

Expectant Motherhood. By Nicholson J. Eastman, M.D., Professor of Obstetrics in Johns Hopkins University, Baltimore. Cloth. Price, \$1.25. Pp. 176, with 9 illustrations. Boston: Little, Brown & Company, 1940.

This is another of the numerous books which have appeared during the last few years attempting to educate expectant mothers about pregnancy and labor. Not only has the author admirably succeeded in presenting this information in simple language, but throughout the book he allays possible fears and explains away absurd ideas and superstitions connected with childbirth. Every woman who reads this or a similar book will find out what occurs to her and her baby during pregnancy and labor. Furthermore, it will make her realize the great value of good antepartum care and the importance of selecting a good physician and a satisfactory hospital for her confinement. This book should be recommended to women who plan to have a baby.

Preventive Medicine. By Mark F. Boyd, M.D., M.S., C.P.H., Field Staff Member, International Health Division of the Rockefeller Foundation. Sixth edition. Cloth. Price, \$5. Pp. 588, with 168 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

The publication of the sixth edition of this standard textbook of preventive medicine is evidence both of the esteem in which it is held and the rapid progress of development in the field of public health. Its greatest usefulness is as a textbook in courses on preventive medicine in medical schools and universities and as a guide to physicians whose public health activities are largely incidental to clinical practice. The book has recognized standing.

The Early Diagnosis of the Acute Abdomen. By Zachary Cope, B.A., M.D., M.S., Surgeon to St. Mary's Hospital, Paddington. Eighth edition. Cloth. Price, \$3.75. Pp. 257, with 36 illustrations. New York & London: Oxford University Press, 1940.

This edition of Cope's famous monograph embodies few additions. Little can be said in further praise of this small but justly popular book that has not already been said in past reviews. A compact volume, it treats with utmost clarity the entire subject of acute conditions of the abdomen. Particularly excellent are the chapters on the method of examining the abdomen and the opening chapter on the principles of diagnosis. The importance of a detailed history is emphasized. Charts illustrating the reference of pain and manual methods of examination are distinctly helpful. Anatomic considerations are utilized to explain the basis for the various diagnostic procedures.

Well known to most, it should be pointed out that this volume has a place on the shelf of every student, surgeon and physician whose work may be even remotely related to pathologic conditions of the abdomen.

The Unseen Plague—Chronic Disease. By Ernst P. Boas, M.D., Chairman, Committee on Chronic Illness Welfare Council of New York City. Cloth. Price, \$2. Pp. 121, with 2 illustrations. New York: J. J. Augustin, Publisher, 1940.

As an administrator of a hospital a large part of which is devoted to the care of the chronically afflicted, as a clinician and as chairman of a permanent committee on chronic illness of the Welfare Council of New York City the author has had ample opportunity to study the various phases of the problem with which he deals. With the exception of mental diseases, tuberculosis and to a certain extent cancer, adequate provision has not been made anywhere for the care of the legions of sufferers from the diverse disabling and crippling illnesses. The book deals comprehensively and conscientiously with the medical, social and organizational aspects of the situation; it takes a discouraging view of the preventive possibilities which lie mainly in popular education and in clinical and laboratory studies on the causes and methods of treatment of the degenerative diseases. According to the author, only improved socio-economic conditions can bring about a real remedy. He develops this point of view in the chapter on public responsibility for the chronic sick, on page 47 of which he says rather impetuously:

An aroused community, in self preservation as well as for humanitarian reasons, must face the fact that the bare existence forced on so large a proportion of our population generates and accelerates disease and undermines the health of vast numbers of citizens. Steady employment, fair wages and proper housing will prevent more disease than most laboratory research and educational ballyhoo about disease prevention.

Neither such occasional outbursts as the one quoted nor the few minor statistical inaccuracies and some inconsistencies of statement detract from the value of the book and the serious challenge it presents to the medical profession and to every thinking man and woman. The best written chapter is that on the aged, and the one dealing with the community program for the care of the chronic sick is the most constructive. The book is provocative of thought and may stimulate not only interest in the problem but action to deal with it in a way its gravity demands.

Psychology and Psychotherapy. By William Brown, D.M., D.Sc., F.R.C.P., Hon. Consulting Psychologist, Bethlem Royal Hospital, Beckenham, Kent. Fourth edition. Cloth. Price, \$4.75. Pp. 260. Baltimore: William Wood & Company, 1940.

The publication of a fourth edition of this little book is ample evidence of its reception and appraisal. The contents frankly and unequivocally deal with psychiatry from a psychoanalytic point of view. Nevertheless, the contributions of all the great schools of psychology are considered and utilized when applicable. This is an excellent introductory book for students of psychiatry.

The Sexual Perversions and Abnormalities. By Clifford Allen, M.D., M.R.C.P., D.P.M., Physician in Charge of the Psychiatric Department of the Seamen's Hospital, Greenwich. Cloth. Price, \$2.25. Pp. 193. New York & London: Oxford University Press, 1940.

The author has with great courage attempted to consider the sexual perversions with a view to indicating the possibilities of therapy for them. His clinical material indicates a wide experience and his therapeutic results by a diversity of methods seem to have been gratifying. The possibilities of cure or amelioration of perversions without lengthy psychoanalysis are convincingly presented by the author from his own material.

La fotografía de las membranas profundas del ojo. Por Manuel de Rivas Cherif. Paper. Pp. 75, with 52 illustrations. Mexico: La Casa de España en México, 1940.

In this booklet there is a brief review of the history and optics of some of the more important cameras used in photographing the fundus of the eye. The pamphlet is well printed on good paper. The diagrams of the cameras and the optical aspects are not bad but the pictures of the fundi are so hopeless that they seem to have been developed under the influence of Rivera. The two color plates are worst of all, the fundus being depicted as a sickish pink-brown.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Reactivated Tuberculosis an Occupational Disease.—The employee in this case had pulmonary tuberculosis which had been in an inactive stage for some sixteen years. He was employed as a grain scooper, which work required him to go into the holds of grain ships and there to operate steam shovels by which the grain was brought within the reach of moving buckets. In the holds of such ships the air was impregnated with minute particles of husk, mustard-seed and dirt. Some time about the middle of the year of 1934 the employee began to have difficulty with his breathing, and his dormant tuberculous condition became reactivated. By June 15, 1936, he became totally disabled and filed a claim for compensation under the longshoremen's and harbor workers' compensation act. The commissioner awarded compensation, the United States district court for the western district of New York affirmed that award and the employer appealed to the United States circuit court of appeals, second circuit.

There was sufficient testimony, in the opinion of the court, to justify the conclusion that hard manual work done for long periods in dust-laden atmosphere tends to produce fibrosis of the lungs, which in turn weakens resistance to any latent tuberculous infection and reactivates that infection. This is what happened in the present case. The important question before the court was whether or not the disability was an injury arising out of employment. If so, it was either an "accidental injury" or an "occupational disease." The court agreed with the commissioner making the award in the first instance that it was an occupational disease. The court was of the opinion that the compensation act should not be extended so as to make it a general health insurance and that to avoid this the coverage must be limited to diseases resulting from working conditions peculiar to the calling. In order to recover a workman must, the court continued, be exposed to hazards greater than those involved in ordinary living, and the disease must arise from one of these hazards. But, although it must be found that special dangers exist in the employment and that the disease arises from such dangers, the court could see no reason for limiting the protected class to those who have a normal resistance to such diseases or for excluding those who are abnormally vulnerable. It might be desirable that the second group should not be employed under such conditions at all, but members of that group may not be charged with ignorance, carelessness or acceptance of the risk because they are. Such considerations, the court pointed out, are alien to the underlying theory of workmen's compensation, which makes industrial disabilities, so far as they are truly attributable to the industry, a part of the cost of production and throws compensation for them on the consumer. This is not because the consumer is at fault for creating the demand whose supply produces the disabilities but because a loss shared among many is less a loss than if borne by one. Since all who actually work in the industry are necessary to the supply, the injuries of all, whether or not they are normally resistant to the unwholesome conditions pervading it, are part of the cost of producing that supply, and compensation for them is within the scheme. It would be an especially harsh interpretation which would exclude just those who are most in need of protection.

The court could see no difference between an acute infection and the awakening of an old one. The compensation act is not concerned with pathologic conditions but with industrial disability; a disease is no disease until it manifests itself. Few adults, the court said, are not diseased, if by that is meant only that the seeds of future troubles are not already planted, and it is commonplace that health is a constant warfare between the body and its enemies. An infection mas-

tered, though latent, is no longer a disease, industrially speaking, until the person's resistance is again so far lowered that he succumbs. It was contended that so broad a construction of the compensation act would result in premiums going to prohibitive heights or that all persons who enter a calling must be examined and the weaker ones excluded. It is possible, the court answered, that the added cost of the system will so raise prices as to throw some workmen out of employment, but so far as it is true one must choose between cheaper and larger production, carried on with less regard for the producers, and a restricted output made under better conditions. Whatever the proper path, the court concluded, it was not for the courts to plot it, and it was enough that the award in the present case seemed to the court to carry out the scheme of the compensation act and fall fairly within the language chosen to embody it. The award in favor of the employee was therefore affirmed.—*Grain Handling Co., Inc., v. Sweeney, 102 F. (2d) 464.*

Malpractice: Death of 6 Year Old Boy Attributed to Chiropractic Adjustments.—Contending that the death of her 6 year old son was due to the carelessness and negligence of the defendant chiropractor, the plaintiff brought suit and obtained a judgment for \$10,000. The defendant then appealed to the district court of appeal of California.

The plaintiff, according to her testimony, first noticed that her son was "stooping a bit." He complained that it had been painful for him to stand erect since a boy bumped him at school. Later a weakness of the legs developed and the plaintiff and her husband took the child to the defendant chiropractor. After roentgenograms had been taken the defendant, according to the plaintiff's testimony, attributed the boy's condition to a misplacement of a vertebra. He then proceeded to give an "adjustment" and continued this form of treatment about every three days for nearly four months, until the boy died. After four or five adjustments the boy developed a temperature of about 100 F. During the course of treatment he lost vitality, weight and color, he complained of pain when the adjustments were being given, and "paralysis was coming from the legs to the arms, and he was completely paralyzed."

From time to time the plaintiff had conversations with the defendant with respect to the child's condition, and the defendant assured her that it was not necessary to call in a doctor because "the only thing the boy had was a certain pressure on the spinal cord, on account of the misplaced vertebra, and he was doing the best thing, and nothing more could be done for the child." The defendant was called as a witness by the plaintiff and he testified that he took roentgenograms of the boy's spine and found "a subluxation of the second cervical vertebra, impinging the nerves, and causing a congestion in the cord," as well as a "rotation of the second, third and fourth cervical." He admitted that he had made no laboratory tests, urinalysis, blood count or other test except the roentgen study and an examination of the spine with his hands, and he found no abnormality, swelling, tumor, contusion or abrasion other than the condition of the second cervical vertebra. He then testified, in part, as follows:

Q.—Did you make any diagnosis of his condition at that time? A.—In chiropractic, we don't use the term "diagnosis." I take it that you want to know if I placed a name on his condition?

Q.—Yes. I want to know if you came to a conclusion? A.—Yes, I came to a conclusion, but in chiropractic we term it "analysis" instead of "diagnosis." . . . My analysis was that he had a subluxation of the second cervical vertebra, causing an impingement of the nerves at that point.

Q.—Well, was that an impingement of the nerves or of the cord? A.—Well, it might have been from both. It was apparent from his condition that there was inflammation of the cord. The inflammation might have been from pressure on the spinal nerves, or upon the cord itself.

Q.—So, it was your finding and your conclusion that at all times, from the time of your first treatment to the last, there was some inflammation and congestion of the spinal cord at the region of the cervical vertebrae? A.—Yes.

A physician associated with the office of the county coroner testified that an autopsy which he performed on the body of the boy "showed the body thin, the lungs congested, the left lung being pneumonic, and both lungs studded with small

tubercles. The heart, liver and stomach were normal. . . . There was no evidence of spinal or other injury. . . . I had been informed that there was some spinal condition existing, and I therefore examined the spine to see if I could find any abnormality, which I did not find." He further testified that in his opinion the boy during the early stage of his illness had tuberculosis of the meninges of the brain, or coverings of the brain. "At that time," this witness testified, "he showed paralysis, which is a typical symptom of early meningitis." In reply to a question as to what effect a chiropractic adjustment of the second cervical vertebra would have when tuberculosis of the spine exists he replied: "It would be detrimental, as rest and quiet would be absolutely indicated in those cases" and that the adjustment would accelerate or increase the existing inflammation. Another doctor of medicine testified that the boy had "some form of meningitic irritation, probably tuberculous in character," and that he was probably suffering from a secondary tuberculosis of the spine. All these witnesses agreed that the chiropractic adjustments were contraindicated and that if the boy had received proper medical attention his chances of recovery would have been good. "I would say that the child died because of lack of proper medical attention, sanitary care and proper fixation," one of the witnesses testified.

In the opinion of the district court of appeal, there was substantial evidence in the record from which the jury could infer that the course of treatment persisted in by the defendant was not of that degree of care, diligence and skill possessed and used by prudent, skilful and careful practitioners of medicine practicing in the same vicinity. The court disagreed with the defendant's contention that the testimony of the doctors of medicine called by the plaintiff should have been excluded because they were not chiropractors. In so holding, the court quoted from *Hutter v. Hommel*, 213 Cal. 677, 3 P. (2d) 554:

We might add that we are cited to no rule obtaining in this jurisdiction and know of none which would preclude a physician trained in one medical school from testifying in a proper case as to the treatment rendered by a physician or surgeon trained in a different school. Such a rule might be promulgated where charges of negligence in a malpractice case are directed toward some special course of treatment to be tested by the general doctrine of a particular school, but it is not applicable to a case of this character where the alleged malpractice is based upon general charges of negligence relating largely to matters of almost common observation within the experience of every physician and surgeon.

The court could find no error in the record and therefore affirmed the judgment for the plaintiff.—*Abos v. Martyn* (Calif.), 88 P. (2d) 797.

Malpractice: Liability of Physician and Municipality to Patient in Municipal Institution.—A New York statute (Consol. Laws, ch. 24, section 50-d) imposes on a municipality ultimate liability for personal injuries sustained by reason of the malpractice of a physician or dentist while rendering services gratuitously to any person in a public institution maintained in whole or in part by the municipality. In the judgment of the Court of Appeals of New York, this statute creates a new remedy against the municipality in favor of the injured person. A physician or dentist who renders services to patients in such an institution and is negligent may still be sued on his common law liability for malpractice, but he has the right to insist that in accordance with the statute he be saved harmless by the municipality. The effect of any action, whether brought against the municipality or the physician or dentist, is determined by the provisions of the statute, and such action may be maintained only if the provisions of the statute relating to commencement of action and filing of notice of intention to commence action against the municipality are complied with strictly. Accordingly, the court held that the trial court had not erred in granting the motion of the defendants, a physician and others charged with malpractice incident to rendering services to a patient in a municipal institution, that the complaint be dismissed because the plaintiffs had failed to comply with the provisions of the statute pertaining to commencement of action and the giving of notice to the municipality of institution of suit. Judgment for the defendants was therefore affirmed.—*Derlicka et al. v. Leo et al.* (N. Y.), 22 N. E. (2d) 367.

Society Proceedings

COMING MEETINGS

American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 19-21. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.
American Society of Anesthetists, New York, Dec. 12. Dr. Paul M. Wood, 745 Fifth Ave., New York, Secretary.
American Student Health Association, Ann Arbor, Mich., Dec. 27-28. Dr. Ralph I. Canuteson, University of Kansas, Lawrence, Kan., Secretary.
Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.
Eastern Section, American Laryngological, Rhinological and Otolological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.
Middle Section, American Laryngological, Rhinological and Otolological Society, Chicago, Jan. 27. Dr. Walter H. Theobald, 307 North Michigan Blvd., Chicago, Chairman.
Puerto Rico, Medical Association of, San Juan, Dec. 13-15. Dr. David E. Garcia, P. O. Box 3866, Santurce, Secretary.
Society of American Bacteriologists, St. Louis, Dec. 27-29. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
Southern Section, American Laryngological, Rhinological and Otolological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.
Southern Surgical Association, Hot Springs, Va., Dec. 10-12. Dr. E. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
Texas Ophthalmological and Oto-Laryngological Society, Fort Worth, Dec. 13-14. Dr. Dan Brannin, Medical Arts Bldg., Dallas, Secretary.
Western Section, American Laryngological, Rhinological and Otolological Society, San Francisco, Feb. 1-2. Dr. Robert C. Martin, 384 Post St., San Francisco, Chairman.

THE AMERICAN RHEUMATISM ASSOCIATION

Seventh Annual Meeting, held in New York, June 10, 1940

DR. LORING T. SWAIM, Boston, Secretary

Mono-Articular and Pauciarticular Arthritis in Children

DR. WILLIAM T. GREEN, Boston: This report concerns a study of children with mono-articular arthritis involving the knee, and pauciarticular (paucitas, Latin, a small number) arthritis in which more than one and not exceeding four joints were involved. In all, forty-three instances of arthritis of the knee and thirty-five of pauciarticular arthritis were studied.

The results to date may be thus summarized: In the Boston area arthritis of mono-articular and pauciarticular type in children is more commonly nonspecific than due to syphilis or tuberculosis. In the pauciarticular and, to a lesser extent, in the mono-articular series, instances in which the symptoms and signs in the joints did not persist over two weeks were frequently found by later determinations to have been due to rheumatic fever. In both groups, when the symptoms and signs persisted over two weeks, they were likely to be prolonged with an average duration of 1½ years. In many of the cases of longer duration the relationship to atrophic arthritis was suggested because the joint manifestations in a large number of the patients were similar to those seen in generalized atrophic arthritis and because three patients in the pauciarticular and one in the mono-articular groups developed generalized atrophic arthritis after a quiescent period of several years. Lengthening of the involved extremity was a common feature in both groups. In twelve of the cases in which the knee was involved there was an average lengthening of 1.3 cm. with squaring of the epiphyses. The treatment, in mono-articular and pauciarticular arthritis of long duration, should be that used in atrophic arthritis. Traction is ideal to correct deformity and develop motion.

DISCUSSION

DR. J. ALBERT KEY, St. Louis: Long ago I heard Dr. Osgood say "When confronted with chronic progressive mono-articular arthritis in a child, the diagnosis is tuberculosis until proved otherwise." I still believe that statement. I do not know what toxic arthritis is. These cases impress me as infectious. Some of them may turn out to be rheumatic fever. Some of them may be true Still's disease. Surgery might be of value if one was assured that they would become chronic. Synovectomy might be definitely indicated. Synovectomy would prevent deformity; it might prevent recurrence, and it might cure the disease. What other treatment besides high vitamin diet does Dr. Green advocate and on what basis was a low carbohydrate diet given?

DR. WALTER BAUER, Boston: Arthritis confined to one or two joints in children is all too frequently called toxic arthritis, a vague, meaningless diagnostic label. Evidently the situation in children is not unlike that in adults, namely that a certain percentage of patients with a mono-articular or "pauciarticular" arthritis are suffering from an atypical form of rheumatic fever or rheumatoid arthritis. What the others represent can be told only by the passage of time and further follow-up studies. It is important to appreciate that joint involvement in rheumatoid arthritis is not always symmetrical, particularly at the onset. Thirty per cent of our patients were atypical in this respect. Until our knowledge of joint diseases is greatly enhanced, the use of the term toxic arthritis is equivalent to saying we do not know. Such being the case, is it not preferable that we label them diagnosis unknown and hope that continuous follow-up study will give us the correct answer in many instances?

DR. M. H. DAWSON, New York: Were antistreptolysin titers determined on these patients? Some of the cases in this group which eventually clear up without residual joint changes are possibly atypical manifestations of rheumatic fever.

DR. WILLIAM T. GREEN, Boston: The antistreptolysin titers have not been determined. I treat this type of arthritis of longer duration exactly as atrophic arthritis. The same problem is involved. In those of briefer duration, the same preliminary treatment should be adopted as that for rheumatic fever. The local treatment in the chronic group involves the active correction of the deformity. Traction applied to the joints allows correction of the deformity and active painless motion. Perhaps one of the reasons why joints do better under such a regimen is that motion stimulates absorption from the joints, as has been shown by Bauer and others. There is no definite justification for any dietary regimen in arthritis, yet in the majority of instances I have recommended a low carbohydrate and high vitamin diet. The general health of these children must be promoted in all possible ways. The best "medicine" is rest.

Heberden's Nodes: Heredity in Hypertrophic Arthritis of the Finger Joints

DR. ROBERT M. STECHER, Cleveland: The present study, confined to idiopathic nodes in white women, is an analysis of the families of sixty-four individuals with Heberden's nodes. All index cases were examined personally. Information about relatives was obtained by examination when possible, otherwise by correspondence or through the family history. Fathers and brothers are not included. Of sixty-two mothers of women with Heberden's nodes, twenty were said to be affected compared to 10.3 which would be found in the general population of a group of the same size and age distribution. In 117 sisters of affected people thirty were found to be affected, compared to 10.3 which would be the expectancy in the population in general. Among 109 sisters of unaffected people in a control series the condition occurred five times compared to an expectancy of 6.26. Various family combinations were noted. Of sixty-two families the mothers were involved twenty times. Three generations of women in direct descent were found in three families. Twelve families had more than one daughter affected. In only twenty-seven of the sixty-four families studied was no evidence of familial involvement discovered. In three families with multiple involvement the probability of such combinations occurring in the same family by chance alone were found to be 1 in 190, 1 in 4,500,000 and 1 in 10,000,000 families. As Heberden's nodes is essentially a disease of later life, it seems unlikely that a common environmental factor was responsible for the condition in several members of the same family. The condition found among families of patients with Heberden's nodes is best explained by a strong hereditary influence.

DISCUSSION

DR. MORTON D. SCHWEITZER, New York: There is a substantially higher incidence among the sisters and mothers of the index cases than in the control series. I should reckon the probabilities in the three pedigrees differently. The total probability in a family is the sum of the probabilities of each member. By this method the results would also appear significant, although smaller than Dr. Stecher finds. I regard this as suggestive of a possible hereditary basis, but not proved, since the other factors suggested by Dr. Stecher as possibly operating in this condition

might also occur more frequently in the family group. There are several technics appropriate for this type of study. A "gene frequency" analysis is particularly useful in the study of conditions which occur as frequently in the population as do Heberden's nodes. Since it is difficult to get all members of the family into the clinic for study, mother-daughter correlations might prove of value. Dr. Stecher, is there any possible relationship between traumatic and idiopathic nodes to be considered and may there be common susceptibility factors underlying the two types? With regard to the sex, the principal difference in the tables is a delayed onset in males of about ten years, in comparison with females.

DR. HOMER F. SWIFT, New York: Has Dr. Stecher analyzed the susceptibility of these patients to trauma? Are their hands specially exposed to injury? From the hereditary standpoint were the siblings compared with the patients in reference to exposure to functional trauma? This factor would be different in a man working in an office and using a pencil and in a scrub woman or a stone mason. In several cases recently observed one or two finger joints specially subjected to functional trauma developed arthritis while the less vigorously used joints remained normal.

DR. J. ALBERT KEY, St. Louis: There is a strong hereditary factor in hypertrophic arthritis. Trauma may produce it experimentally, but clinically there are a great many cases in which it is not produced by trauma. Heberden's nodes are seen in old ladies who have done no manual work in their lives.

DR. RUSSELL L. CECIL, New York: Both my father and my mother developed Heberden's nodes in the fifties. I have no Heberden's nodes. I have tried to explain this in various ways. My father was raised on a farm and, as a young man, used his hands a great deal; then he became a clergyman and used his hands but little. My mother was energetic, always sewing or darning, and used her hands a great deal. The only hard use I ever put my hands to is playing golf. My feeling is that the reason I have not developed Heberden's nodes is that I have not used my hands. I think the condition is largely the result of trauma.

DR. CURRIER MCEWEN, New York: It has been said that if trauma does play a role we should see Heberden's nodes especially in stenographers who reach the age at which osteoarthritis is common. I have not been struck by any undue occurrence of Heberden's nodes in people who used their hands in laborious work in their earlier days. This raises in my mind the question just what part trauma plays in Heberden's nodes. Three of my patients have Heberden's nodes on one hand and not on the other. In the hand in which they do not occur there had been peripheral nerve injuries with quite obvious trophic changes in the skin. In one of these patients three fingers are useful and two are paralyzed on the injured hand. There are marked Heberden's nodes on the good hand and moderate ones on the usable fingers of the injured hand, but no sign of them on the paralyzed fingers. I wonder if that speaks for the traumatic theory, since these fingers cannot be used and hence are spared trauma, or whether some trophic change prevents the formation of the nodes on those fingers.

DR. HOMER F. SWIFT, New York: In studying the influence of trauma on the causation of disease one is liable to emphasize that inflicted by external or physical forces and to neglect that arising from internal or functional factors. Drs. Smadel, Farr and I have studied this question in the induction of chronic nephritis in rats and have found that hereditary and functional traumatic factors are both important and cooperative. Acute nephrotoxic nephritis was induced in rats; when the work the kidneys performed was reduced to a low level the nephritis disappeared. When, on the other hand, the diet contained sufficient protein to maintain a normal rat in health, i. e. 18 per cent nitrogen, and the kidneys were forced to excrete that amount, one strain of rats developed severe chronic progressive nephritis. In two other strains this tendency was less marked, and chronic kidney disease was best induced by an abnormally high protein diet. In stating my original question, therefore, I did not wish to neglect the influence of heredity in the induction of arthritis but to emphasize the contributory influence of functional trauma. A full analysis of etiology would doubtless embrace both factors

as well as others, and only by keeping alert to all possibilities will one determine the ultimate answer.

DR. DAVID H. KLING, Los Angeles: Would Dr. Stecher clarify the definition of Heberden's nodes? Does he classify spur formations visualized by x-ray examination as Heberden's nodes as well as new bone formation seen in hypertrophic arthritis or does he designate any kind of swelling of the phalanges as Heberden's nodes? I have seen periarticular cystic lesions containing a gelatinous fluid that persist for years with no evidence of bony spur formation. Perhaps in these cases trauma may provoke cystic lesions, owing to degeneration of the soft periarticular tissues.

DR. PHILIP S. HENCH, Rochester, Minn.: One of my patients, an elderly woman, had had infantile paralysis as a child with resultant partial paralysis of one arm and hand. Despite persistent atrophy and arrested development of this hand she had slowly regained considerable use of it, probably 50 per cent normal. Years later definite Heberden's nodes developed on the fingers of her normal hand but not a sign of them appeared on the partially paralyzed extremity. Does this not suggest that some trophic factor, rather than mere age or trauma, plays a role in the production of Heberden's nodes?

DR. RALPH PEMBERTON, Philadelphia: There are many factors in the situation which have not been analyzed as yet and are possibly not susceptible to analysis. Thus when one considers familial incidence one must also consider topographic and geographic factors as well as traumatic and nutritional influences. However, there are probably few who can escape the conviction of at least occasional familial trends operative in both major aspects of the problem. In a series of 500 cases which my associate Dr. Bach and I have been studying, the evidence of hereditary influences is almost the same in the two major groups, namely atrophic 50 per cent, hypertrophic 42 per cent, mixed type 44 per cent. The relationship which Heberden's nodes bear to the syndrome of hypertrophic arthritis as a whole is perhaps not wholly clear. Dr. Stecher's remarks, however, coincide with the views of those who find it difficult to believe that hypertrophic arthritis is a manifestation of age and trauma alone.

DR. ROBERT M. STECHER, Cleveland: I hope that the more technical methods of genetics which Dr. Schweitzer has discussed can be applied to these data with profit. Tentatively Heberden's nodes seem, at the present time, to be inherited as a single chromosome factor which is sex influenced, being dominant in females and recessive in males. This lacks substantiation. Dr. Pemberton has mentioned other possible factors of etiology. Common environment is pretty well ruled out because Heberden's nodes occur in middle and late life long after sisters have ceased to live together. A common environment does not account for occurrence in three generations. Climate was not considered in the study on incidence. This study was confined to Cleveland, to people of the working class who attended public clinics. In the family studies, sisters were widely separated geographically. Social and economic differences were not considered in the incidence studies. However, I feel certain that inclusion of members of the leisure or wealthy class to the proportion in which they occur in the population in general would not materially affect the incidence statistics. My conclusions concerning trauma may seem rather dogmatic but they are based on extended inquiry from many affected persons. Traumatic arthritis of one finger or of several fingers on the same hand occurs after definite injury, a single episode of such severity that it is definitely recalled. I do not believe that it is proper to confuse trauma with ordinary use and function. Playing a piano or using a typewriter should not be considered trauma. Dr. Kling asks whether heredity plays a role in hypertrophic arthritis. The most that has been found in the literature is that hypertrophic arthritis runs in families or that 20 per cent of the families show more than one involved member. Such statements mean little because no information is available as to the proportion of involved to noninvolved persons in these families. Dr. Cecil has not told us how many siblings were born or lived to an age when Heberden's nodes might be expected in his family. If my theory is correct and the condition is recessive in males, we would expect only one half the men to be affected if the mother was heterozygous, all the men affected if the mother

was also homozygous. If the father has Heberden's nodes, one would expect all his daughters to be affected regardless of the condition of the mother. I have seen one case similar to that described by Dr. Hench as well as another with peripheral nerve injury. The first of my patients had a daughter with Heberden's nodes, the second had a sister with Heberden's nodes. Three cases have been described in the literature of Heberden's nodes appearing after the patient suffered a hemiplegia. In these instances the healthy side alone was affected. Two patients had hemiplegias after Heberden's nodes had developed. After about a year's duration, no observable change has been noted in the nodes on the paralyzed side. I do not believe that trauma plays any part in such cases.

Local and Regional Analgesic Injections in the Treatment of Intractable, Nonsurgical Shoulder Conditions

DR. OTTO STEINBROCKER, New York: Analgesic solutions have been used for the past four or five years for diagnosis and treatment in arthritis and related musculoskeletal disease in the clinic in which I work. This report embraces our therapeutic experience with analgesic injections for the disabled shoulder. Before such treatment is undertaken complete examination, in doubtful instances necessary studies to rule out visceral pain, at least a tentative diagnosis, and a course of the usual medical and physical therapy are carried out as a matter of routine. Only a small percentage of affected shoulders were so refractory to other, accepted measures as to require analgesic injection. This treatment may be accomplished by (1) local, deep deposit of medication at the site of maximum tenderness, (2) regional supraclavicular brachial plexus block, (3) cervicodorsal paravertebral nerve block or (4) sympathetic (stellate ganglion) injection. The sympathetic approach is required occasionally for postherpetic and postamputation neuralgias. In the last few years we have had to resort to the paravertebral cervical block in only three cases.

Local injection at the site of maximum tenderness was employed for circumscribed fibrositis (fibromyositis, myofascitis, myositis) about the shoulder and neck, peripheral neuralgia and subdeltoid bursitis. In the majority of cases such treatment produced lasting effective results when the symptoms were due to referred pain. Local lesions were accompanied in some instances by secondary pain and tenderness in a surrounding halo or referred down the extremity. The secondary symptoms also responded when the peripheral source of trouble was correctly located and infiltrated. These circumscribed, peripheral disturbances often were eliminated by from one to ten injections of 2 to 15 cc. of 1 per cent procaine hydrochloride or equivalent aqueous solutions at intervals of from one to twenty-one days. In stubborn cases from 1 to 5 cc. of 2 per cent procaine base in oil was used. When repeated local injection failed, reconsideration of the diagnosis became necessary and brachial plexus block was utilized, when indicated.

We have found the supraclavicular brachial plexus block, with the Labat technic, a practical and effective procedure applied in our clinic without complication to ambulatory patients presenting intractable pain and disability of the shoulder region. The disorders treated by this method were diagnosed in the order of frequency as fibrositis of the periarticular and neck regions, osteo-arthritis of the cervicodorsal spine with referred symptoms, subdeltoid bursitis, rheumatoid arthritis (inactive), cervicobrachial neuralgia (due to pressure from fibrositis about the plexus or scalenus anterior involvement?) and osteo-arthritis of the shoulder joint (coraco-acromial, scapulohumeral). The conditions included in this group show a more or less identical symptom pattern dominated chiefly by pain referred down the extremity with limited abduction and rotation.

The severity of these symptoms in each case reflects the progress of the vicious cycle common in musculoskeletal disorder—pain, muscle spasm, postural deficiency, disability, deformity and trophic disturbances. According to our experience the cycle may be alleviated or abolished in selected cases by the use of the brachial plexus block with procaine solution. This technic was employed by us whenever possible in conjunction with manipulation, exercise and physical and medical measures which frequently had proved ineffective before blocking. Of seventy-six patients with intractable, usually chronic, shoulder

disorders, 73 per cent were greatly to completely relieved of symptoms and disability after from one to fourteen injections, averaging six, of 20 to 40 cc. of 1 per cent procaine solution or equivalent medication given at intervals of two to seven days.

DISCUSSION

DR. EZRA LIPKIN, Detroit: Following the publication of Dr. Steinbrocker's article in the *Annals of Internal Medicine* of June 1939 I injected 100 patients suffering from so-called rheumatic conditions with aqueous and oily solutions of procaine hydrochloride. Among these were forty-five patients with periarthritis of the shoulder, with negative x-ray appearances, who were treated by means of brachial block. The chief complaints were pain in the shoulder and arm, and limitation in abduction and external rotation. Following a number of regional injections of 1 to 2 per cent aqueous procaine hydrochloride solution—the average being three—there resulted either complete recovery or marked improvement in thirty-three of the forty-five patients, or 73 per cent—a figure which coincides exactly with that obtained by Dr. Steinbrocker. The period of observation extended up to eleven months. The anesthesia in the arm following the injection of the brachial plexus lasted from two to three hours and gave way to analgesia lasting from four to seven days or longer in some cases. Subsequent injections diminished the pain still further until there was complete remission or marked improvement of the symptoms. The one remarkable feature observed in the brachial block injections was the almost immediate relaxation of muscle spasm. I did not follow the injections with passive manipulation. Rather, the patient was encouraged to engage the arm in active exercise, which, because of freedom from pain, he was now able to perform. There were no untoward effects except for transient dizziness and numbness in the arm. When the brachial plexus is touched, the patient experiences a sudden, electric-like sensation in the arm. The solution is injected at this point. I used from 10 to 12 cc. of aqueous solution of procaine, although amounts up to 30 cc. have been recommended. Better results can be expected when the solution is injected directly into the nerve plexus rather than around it. Originally I employed the technic of Labat, injecting the solution in three areas, radiating from the single intradermal wheal 1 cm. above the midclavicle. To minimize trauma I reduced the number of points injected to one, namely, that aimed at the first rib. The results appeared to be as satisfactory as when the three injections were used, provided the brachial plexus is infiltrated, rather than the tissues around it.

DR. E. A. ROVENSTINE, New York: Nerve block or local infiltration procedures with analgesic solutions in painful non-surgical conditions as a therapeutic or diagnostic measure is rapidly gaining a wide and more important usefulness. Local anesthetization is no cure-all for somatic pain. The procedure should never be substituted for an extensive attempt to discover the cause of pain and never be performed, unless as a diagnostic measure, until such an attempt has been made. As a more accurate neuro-anatomic approach to the problem of shoulder pain my associates and I block the suprascapular nerve at the lesser scapular notch. Our desire for blocking the nerve is based on the knowledge that its sensory components form a vital pathway for pain fibers from the scapulohumeral and acromioclavicular joints and periarticular structures about the shoulder joint. The articular and periarticular branches leave the nerve in the supraspinatus and infraspinatus fossae, so that to obtain interruption of all the sensory impulses transmitted over the nerve it is ideally blocked at the suprascapular notch. The details of the technic have been worked out in the anesthesia department at Bellevue and the favorable results seen have encouraged its continued use.

DR. J. ALBERT KEY, St. Louis: In my experience people who have analgesic injections for subdeltoid bursitis go home, the anesthesia wears off and then some of them may have terrible pain. With the use of nupercaine and oil it has been shown recently that the patient may get a prolonged anesthesia which goes on to actual degeneration of the nerve and permanent paralysis. My experience has been with the use of procaine in acutely inflamed bursae. Those can be cured. With the chronic conditions I have had relatively little luck, not anything like the percentage shown here.

DR. WILLIAM T. GREEN, Boston: More emphasis should be placed on diagnosis in making decisions as to the type of therapy to employ. In certain cases of back pain we have injected a solution of procaine into the skin over the area which was sensitive to palpation, followed by the disappearance of all tenderness. Most often the relief was temporary, but I have been amazed to see certain patients remarkably improved—though I do not recommend this as fundamental therapy. I do use local irrigations in the therapy of bursitis and tendinitis, as seen most frequently about the shoulder. After preliminary local anesthesia, two needles of 18 or 19 gage caliber are introduced into the calcific area, and through and through irrigation is carried out with physiologic solution of sodium chloride. It is my feeling that the excellent results obtained are due not to the injection of procaine hydrochloride on any analgesic basis but rather to the mechanical factors which are involved. Often calcific material may be obtained from such irrigation and in those cases in which we are unable to obtain it we lay particular stress in multiple needling of the involved area. The results in this procedure are satisfactory, particularly in the acute cases. In general, I am against analgesic injections, particularly of the type represented by a brachial plexus block, unless the process cannot be treated locally or the pain is intractable. It is my experience that passive motion is inferior to active motion or active guided motion in almost all instances.

DR. JOHN P. STUMP, New York: Dr. Steinbrocker has used the term "nonsurgical" in his title. That word means that his patients have been through the hands of internists, orthopedists and neurologists without relief before he has employed his method of nerve block. His results have been gratifying.

DR. A. S. GORDON, Brooklyn: What relation, frequency and association does Dr. Steinbrocker find between painful shoulders and local tender points along the cervical spine of the same side? What experience and success did he have in injecting other joints, particularly the knee joint?

DR. OTTO STEINBROCKER, New York: I consider it wise to avoid injecting directly into a nerve. Occasionally in the course of a routine block a nerve may be traumatized when the needle penetrates it and some later discomfort arises. It is advisable in ordinary therapeutic procedures to employ perineural injections. Of course following any type of block temporary local discomfort may occasionally appear shortly afterward or when anesthesia wears off. When it occurs, this reaction is transient and is thought to be due chiefly to the hyperemia produced. As far as my observation goes, I agree with Dr. Key on the treatment of acute bursitis. The methods I have described were applied to chronic bursitis. Proper diagnosis is a complex problem in many of these cases before blocking is done. It is at times difficult enough to decide on the wisdom and method of injection even after thorough diagnostic study. In some borderline situations, proper block may prove of diagnostic as well as therapeutic value. I try to determine the importance of mechanical factors before I begin treatment. Merely to inject a patient with obvious skeletal defects causing symptoms, or while he is receiving corrective therapy for poor body mechanics, is of course not advisable. Exceptions to this rule are individuals with persistent localized areas of pain and muscle spasm which delay improvement. Injecting such foci of irritation has been found a helpful adjunct, hastening response to other measures. Coronary and other cardiac disturbance complicated or obscured by parietal spine or shoulder symptoms may present difficult problems of diagnosis and treatment. If the complaints are not of cardiac origin, I use whichever procedure is indicated for the musculoskeletal condition. Unless moribund, the average cardiac patient takes block well and the resulting relief of discomfort helps in every way. If the pain is thought to be definitely cardiac in origin, particularly coronary, sympathetic (stellate) injection is indicated. If the origin of the symptoms remains doubtful and relief is imperative, local procedures are first used, then brachial plexus block and finally sympathetic injection. The problem of differential block in these conditions is not conclusive at this time. There are many phases of the subject of analgesic injections requiring further investigation and improvement but, correctly applied, those procedures now available are helpful in the relief and control of pain and disability in many conditions.

(To be continued)

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

60:783-1018 (Oct.) 1940

- Prognosis in Postencephalitic Disorders. P. Heersemma, Rochester, Minn.—p. 783.
- Supension Grasp Behavior of the Human Infant. Myrtle B. McGraw, New York.—p. 799.
- *Hemolytic Disease in Infants. A. F. Abt, Chicago.—p. 812.
- Blood Volume and Extracellular Fluid Volume of Infants and Children: Studies with Improved Dye Micromethod for Determination of Blood Volume. M. Robinow and W. F. Hamilton, Augusta, Ga.—p. 827.
- Paranasal Sinuses from Birth to Late Adolescence: II. Clinical and Roentgenographic Evidence of Infection. M. M. Maresch and A. H. Washburn, Denver.—p. 841.
- Intracutaneous Tests with Pertussis "Toxin" and Complement Fixation Tests in Whooping Cough. M. Weichsel, H. J. Rubin, P. Cohen and J. H. Lapin, New York.—p. 862.
- *Disturbances of Hepatic Function in Icterus Gravis: Report of Two Cases. W. W. Zuelzer and J. A. Bigler, Chicago.—p. 873.
- Levels of Sulfapyridine in Blood of Children Following Dosage by Body Weight. G. E. Cullen and Armine T. Wilson, Cincinnati.—p. 891.
- Urine Collector for Female Infants. R. Cohen, Louisville, Ky., and M. L. Blatt, Chicago.—p. 897.
- Adrenocortical Obesity in Children. T. M. Marks, Lexington, Ky.; J. M. Thomas, Omaha, and J. Warkany, Cincinnati.—p. 923.

Hemolytic Disease in Infants.—Abt reports three cases of hemolytic anemia in early infancy. The symptoms in one were observed at birth and in the other two at 4 months of age. A familial history could not be obtained. In early infancy the anemia is often a more pronounced symptom than icterus and is generally severe. The onset of the disorder may be insidious or it may occur as a severe hemolytic crisis and terminate fatally. Splenomegaly is usually of a considerable degree. When symptoms appear early, the first crisis is apt to be most severe. A severe crisis occurred in one of the cases. In the other two there were frequent crises which, though not so severe, necessitated transfusions at intervals of from three weeks to three months. Jaundice may be entirely absent even though there is indisputable evidence of blood destruction. The increase in reticulocytes is considerable. Increased fragility of the erythrocytes has been one of the usual criteria for the diagnosis of the condition. The leukocytes are generally normal or somewhat increased, and the platelets are usually within normal limits. An increase in normoblasts is generally observed. Bilirubinemia is always present. The icteric index is increased, and the indirect van den Bergh reaction is positive. Smears of the bone marrow obtained by sternal puncture reveal an increase in nucleated erythrocytes, a characteristic of hemolytic disease. General glandular enlargement is not usually observed in early infancy and was not present in the author's patients. There were no skeletal changes. Ocular lesions have not been reported in infancy. The crises of the disease show varying degrees of severity and different manifestations. Generally, infants manifest prodromal symptoms (lassitude, lack of appetite and fretfulness) followed by deepened jaundice and increased anemia. Usually during the periods of crisis the spleen enlarges and the urine becomes dark. Abdominal symptoms have not been characteristic of the condition in infancy. Occasionally crises are initiated by febrile attacks, when the symptoms are magnified and the infant may be extremely prostrate. Periodicity in the occurrence of crises is the rule. In one of the infants crisis occurred every three weeks, in another approximately every three months and in the third a single severe crisis occurred. The extent of jaundice and anemia vary considerably from attack to attack. The amount of urobilin in the urine is increased, especially after a crisis. Occasionally hemoglobinuria may be observed. The stools are normal but occasionally dark. Acholia is never present. Blood

transfusion and serum are temporary therapeutic aids which effectively combat an acute crisis. Splenectomy is the permanent therapeutic measure, and its expectant benefits outweigh the operative hazards. Accessory splenic tissue should be searched for and removed at the time of operation. Two of the author's patients have successfully undergone splenectomy at the ages of 15 months and 2½ years, respectively. In the third there has been no recurrent crisis during the ten months following the initial attack, and no splenectomy has been performed.

Hepatic Function in Icterus Gravis.—Zuelzer and Bigler cite two cases to emphasize the importance of hepatic damage in certain cases of icterus gravis neonatorum. The two cases occurred in one family; one illustrates a protracted course resulting in cirrhosis and the other an acute phase of hepatic damage. Both cases were associated with an unusual derangement of carbohydrate metabolism on the basis of hepatic dysfunction which is rarely observed in infants. Both patients died, one after a survival of eight months which finally ended in cirrhosis and the other at the end of the first week of life with kernicterus. Severe fatty changes, hemosiderosis and deposits of bile pigment were found in the liver. No clinical or pathologic evidence of erythroblastosis was present in either case. The metabolic disturbances (insulin-refractory glycosuria, hyperglycemia, absence of ketosis and sensitivity to insulin) are interpreted by the authors on the basis of the pathologic observations as a manifestation of impaired hepatic glycogenesis. After insulin therapy, insulin-like reactions without associated hypoglycemia and anatomic damage to the brain were observed in one of the cases. The possibility of a direct toxic effect of insulin on the central nervous system in the absence of hypoglycemia is considered and a tentative explanation is submitted.

American Journal of Ophthalmology, St. Louis

23:1089-1198 (Oct.) 1940

- Studies on Keratoconus Relative to Effect of Prolonged Application of Pressure. T. L. Terry and J. F. Chisholm Jr., Boston.—p. 1089.
- Effect of Certain Physical and Chemical Stimuli on Caliber of Retinal Blood Vessels in Man. I. Puntene, Chicago.—p. 1113.
- Study of Practical Cycloplegia, with Special Reference to Use of Pare-drine: Review of 341 Cases. E. J. Wenaas, W. H. Evans and R. E. Odom, Youngstown, Ohio.—p. 1123.
- Concerning the Chamber Angle: III. Clinical Method of Goniometry. H. S. Gradle and H. S. Sugar, Chicago.—p. 1135.
- *Homotransplantation of Preserved Cornea: Experimental Study. M. Fine, San Francisco.—p. 1140.
- Inherited Eye Defect in Guinea Pig: Report of Further Anatomic Studies. H. L. Foust, Ames, Iowa.—p. 1146.
- A Pressure Dressing. R. L. Pfeiffer, New York.—p. 1156.

Homotransplantation of Preserved Cornea.—Fine attempted to determine the relative merits of immediate and delayed transplantation of the cornea by controlled experiments on rabbits. Thirty-one animals were given partial penetrating transplants into normal corneas from eyes that had been enucleated at death and preserved for from twenty-four to fifty-two hours at a temperature of 4 C., as described by Filatov. The results obtained were compared with those of a control series of twenty-five rabbits in which homotransplants were performed with corneal tissue removed within twenty minutes after death. In the control group 52 per cent, or thirteen, of the operations resulted in grafts which were transparent to such a degree that the fundus could be seen through the graft. If one third of the transplant showed this degree of transparency, it was considered successful. In four of the thirteen clear grafts there were single narrow anterior synechiae. These did not result in vascularization or opacification of the transplants even after six months. In the thirty-one delayed transplantations (from twenty-four to fifty-two hours) there were ten clear grafts (32 per cent). Of sixteen operations with corneas preserved for twenty-four hours, seven resulted in transparent grafts and of fifteen operations with corneas preserved for forty-eight or more hours only three resulted in satisfactory grafts. The primary causes of opacification in corneal transplants are poor nutrition of the graft, infection, incarceration of the iris in the operative wound and vascularization. Secondary to these causes are poor adaptation of the margins of the graft to the host's cornea, marked early edema of the graft, corneal fistula, pressure from sutures on the surface of the graft, suture infection and folding of Descemet's membrane. When vascularization

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- Physiology of Aviation and Medical Preparedness. J. F. Fulton, New Haven.—p. 590.
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Medical Aspects of Deep Sea Diving. C. W. Shilling, Washington, D. C.—p. 597.
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Diagnosis of Perforated Peptic Ulcer. L. River, Oak Park.—p. 344.
*Treatment of Psoriasis with Various Vitamin D Preparations. E. A. Thacker, New Orleans.—p. 352.

Vitamin D Preparations for Psoriasis.—Thacker used viosterol, crystalline vitamin D, a mixture of western fish oils, a special concentrated cod liver oil in capsules and a stock concentrated cod liver oil internally for the treatment of twelve persons afflicted with psoriasis. Concentrated cod liver oil in a vanishing cream base was applied to the psoriatic areas. The lesions of nine patients disappeared following treatment with the stock concentrated cod liver oil and the special concentrated cod liver oil in capsules. Two patients failed to respond to this therapy and the condition of one was slightly improved. The daily amount of vitamin D in the stock concentrated preparation used varied from 500 to 945 units per kilogram for the fifty-two to the ninety days during which it was given. The special concentrated cod liver oil in capsules required approximately twice this amount before the psoriasis disappeared. The first five persons treated have been free from psoriasis since treatment was terminated about one year ago. Psoriatic lesions failed to regress after the administration of seven or eight times as much vitamin D in the form of viosterol and crystalline vitamin D as that of the concentrated cod liver oil. The areas of psoriasis

occurred in fresh tissue grafts it resulted from the adherence of the iris to the posterior surface of the corneal wound or actual incarceration of the iris. In contrast, with preserved grafts vascularization for the most part was superficial and proceeded from the limbal loops as a result of degeneration of the superficial layers of the graft. Eight iris adhesions were encountered in the control group and five in the series of delayed transplants. The author concludes that until more conclusive evidence of the superiority of preserved cornea for keratoplasty is forthcoming the conservative surgeon will choose fresh tissue, if available, or tissue preserved for a minimal length of time.

American Journal of Physiology, Baltimore
130:421-612 (Sept.) 1940. Partial Index

- Size of Extracellular Fluid Compartment Before and After Massive Infusions. A. M. Lands, R. A. Cutting and P. S. Larson, Washington, D. C.—p. 421.
Posttetanic Potentiation and Suppression in Muscle. L. Grumbach and D. T. Wilber, Ithaca, N. Y.—p. 433.
Anoxic Effects of High Oxygen Pressure on Smooth Muscle. J. W. Bean and D. F. Bohr, Ann Arbor, Mich.—p. 445.
Reduction of Blood Pressure of Hypertensive Dogs by Administration of Renal Extract. J. R. Williams Jr., Nashville, Tenn.; A. Grollman, Baltimore, and T. R. Harrison, Nashville, Tenn.—p. 496.
Distribution of Blood Perfusates in Capillary Circulation. B. W. Zweifach, New York.—p. 512.
Prolonged Action of Acidified Solution of Protamine Zinc Insulin. M. Sahjun, with assistance of A. Nixon, Detroit.—p. 521.
Comparison of Effects of Cold and Thyrotropic Hormone on Thyroid Gland. P. Starr and R. Roskelley, Chicago.—p. 549.
Mechanism of Depression of Serum Potassium Level by Epinephrine. P. S. Larson, Richmond, Va.—p. 562.
Mechanism of Action of Dicarboxylic Acids in Blood Coagulation. G. J. Martin, New York.—p. 574.
Hormone Influences on Carbohydrate Metabolism During Work. E. Asmussen, J. W. Wilson and D. B. Dill, Boston.—p. 600.
Further Observations on Total Chloride Content: Relationship Between Body Fat and Body Chloride. E. G. Weir, Washington, D. C.—p. 608.

Bulletin New York Academy of Medicine, New York
16:605-656 (Oct.) 1940

- Aging of the Cardiovascular System. E. P. Boas, New York.—p. 607.
Histamine in Anaphylaxis and Allergy. L. Farmer, New York.—p. 618.
An American Precursor of Freud. A. A. Brill, New York.—p. 631.

California and Western Medicine, San Francisco
53:153-200 (Oct.) 1940

- Obesity. E. H. Rymearson and Anne Whitcomb Sprague, Rochester, Minn.—p. 158.
Traumatic Appendicitis. G. K. Rhodes and W. D. Birnbaum, San Francisco.—p. 162.
Osteomyelitis of Bones of Face in Severe Diabetic: Recovery and Plastic Reconstruction. M. N. Hosmer, D. K. Burnham and A. D. Davis, San Francisco.—p. 165.
Infantile Eczema: Its Dermatologic Management. F. G. Novy Jr., Oakland.—p. 168.
Epilepsy: General Survey of Convulsive State. J. A. Cutting, Agnew, Pa.—p. 170.
Interpretation of Laboratory Examinations in Diagnosis of Infectious Diseases. C. S. Keefer, Boston.—p. 173.

Canadian Medical Association Journal, Montreal
43:305-404 (Oct.) 1940

- A Decade of Pediatric Progress. A. Brown, Toronto.—p. 305.
Examination of the Recruit. A. R. Hagerman, Toronto.—p. 314.
Medical Aspects of the Air Force. R. W. Ryan, Regina, Sask.—p. 316.
Proposal for More Radical Treatment of Gunshot Wounds of the Brain. G. Horrax, Boston.—p. 320.
Fractures—Elastic Band Traction. S. D. McKinnon, Rouyn, Que.—p. 324.
Surgical Treatment of Flat Feet. G. L. Burke, Vancouver, B. C.—p. 327.
Congenital Hydronephrosis. A. Strasberg, Montreal.—p. 332.
Beneficial Action of Desoxycorticosterone Acetate in Uremia. H. Selye, Montreal.—p. 333.
Problems of the Adolescent Child. A. Goldbloom, Montreal.—p. 336.
Respiration During Anesthesia. M. D. Leigh, Montreal.—p. 340.
Nupercaine Spinal Anesthesia in Abdominal Surgery. A. R. Wilkins, Toronto.—p. 342.
Is Physical Examination of Lungs Worth While? J. D. Adamson, Winnipeg, Man.—p. 345.
People Who Are Always Complaining. A. H. Gordon, Montreal.—p. 349.
Intestinal Obstruction. W. A. Curry, Halifax, N. S.—p. 352.
Dermatologic Neuroses. W. R. Jaffrey, Hamilton, Ont.—p. 356.
Clinicopathologic Correlation Chart for Bright's Disease. S. W. Lippincott, Montreal.—p. 359.
Carcinoma of Cervix in the First Three Decades of Life. N. D. Hall, Phoenix, Ariz.—p. 362.
Essential Unsaturated Fatty Acids in the Relief of the Common Cold. E. M. Boyd and W. F. Connell, Kingston, Ont.—p. 365.

also failed to respond to the mixture of western fish oils. Therefore it appears that cod liver oil contains an unidentified antipsoriatic factor in a greater quantity than is present in the other preparations used. The sequence in the disappearance of the lesions is a profuse coarse scaling which occurs generally within three weeks after treatment is begun followed by thinning, fading of the redness of the base and a fine branlike scaling. After the lesions are gone the formerly involved areas are not to be distinguished from uninvolved areas. Local application of concentrated cod liver oil had no effect on the disorder. Psoriasis is probably due to a metabolic disturbance, the nature of which is yet to be determined.

Journal of Nervous and Mental Disease, New York

92:429-568 (Oct.) 1940

- Bilateral Cortical Thromboses: Report of Case. D. M. Palmer, Columbus, Ohio.—p. 429.
Hypoglycemic Epilepsy. L. J. Robinson, Palmer, Mass.—p. 442.
Degeneration of Basal Ganglions Associated with Olivopontocerebellar Atrophy. C. D. Aring, Cincinnati.—p. 448.
Vigilance and the Vitalistic Hypothesis. S. E. Jelliffe, New York.—p. 471.
Cerebellar Agenesis. H. S. Rubinstein and W. Freeman, Washington, D. C.—p. 489.

Journal of Nutrition, Philadelphia

20:197-304 (Sept.) 1940. Partial Index

- Further Evidence of Mode of Action of Vitamin D. Margaret Cammack Smith and H. Spector, Tucson, Ariz.—p. 197.
Comparative Rate of Absorption of Some Natural Fats. H. J. Deuel Jr., Lois Hallman and A. Leonard, Los Angeles.—p. 215.
Calcium and Phosphorus Content of Certain Vegetables Grown Under Known Conditions of Fertilization. Ernestine Elmendorf and H. B. Pierce, Rochester, N. Y.—p. 243.
Metabolism of Citric Acid by Infants. A. H. Smith, D. J. Barnes, C. E. Meyer and M. Kaucher, Detroit.—p. 255.
Utilization of Calcium in Carrots, Lettuce and String Beans in Comparison with Calcium in Milk. J. B. Shields, B. W. Fairbanks, G. H. Berryman and H. H. Mitchell, Urbana, Ill.—p. 263.
Utilization of Calcium of Dicalcium Phosphate by Children. Elizabeth Kempster, Herta Breiter, Rosalind Mills, Beula McKey, Marie Bernds and Julia Outhouse, Urbana, Ill.—p. 279.
Pectic Enzymes: V. Fate of Pectins in Animal Body. Z. I. Kertesz, Geneva, N. Y.—p. 289.

Journal of Thoracic Surgery, St. Louis

10:1-130 (Oct.) 1940

- Etiology of Thin-Walled Thoracic Cysts. A. V. S. Lambert, New York.—p. 1.
Extrapleural Pneumothorax. E. C. Janes, D. B. Aitchison and A. Forsberg, Hamilton, Ont.—p. 8.
Extrapleural Pneumothorax in Artificial Pneumothorax: Report of Thirty-Three Cases. J. S. Harter and A. A. Lilienthal, Sanatorium, Miss.—p. 14.
Bronchopneumography: I. Description of Catheter and Technic of Intubation. W. A. Zavod, Mount Vernon, N. Y.—p. 27.
Id.: II. Application to Collapse Therapy: Preliminary Report. G. Leiner, M. Pinner, New York, and W. A. Zavod, Mount Vernon, N. Y.—p. 32.
Heart Pain. P. Heinbecker, St. Louis.—p. 44.
*Experiences in Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus. A. S. W. Touroff and H. Vesell, New York.—p. 59.
Individual Ligation Technic for Lower Lobe Lobectomy. B. Blades and E. M. Kent, St. Louis.—p. 84.
*Experiences with Lobectomy and Pneumonectomy in Pulmonary Tuberculosis. F. S. Dolley and J. C. Jones, Los Angeles.—p. 102.

Extrapleural Pneumothorax.—Since November 1937 Janes and his co-workers performed extrapleural pneumothorax on seventy-seven patients. Fifteen have since had oleothorax. The interval between the operation and the replacement of air with oil has gradually decreased. The shortest interval was three months. Despite the fact that a bronchopleural fistula developed in one patient soon after the injection of oil, the staff is becoming convinced that the injection of oil to maintain permanent collapse is desirable in many cases. Because of inadequate collapse one patient had a second operation. The extrapleural space was deliberately combined with a preexisting intrapleural pneumothorax in eight patients. Four of these have made satisfactory progress. Bronchopleural fistulas developed in three and a tuberculous and pyogenic empyema with spread of the disease into the opposite lung in one. The empyema finally cleared and the space is satisfactory, but a cavity persists in the opposite lung. These eight cases suggest that it is not advisable to connect extrapleural and intrapleural spaces unless the location and extent of the disease command it. Three patients have had

thoracoplasties since the extrapleural pneumonolysis. Eight of the seventy-seven patients have died; five deaths occurred within five or less weeks after operation and three were late postoperative deaths. The sputum was converted and the cavity closed in fifty of the sixty-nine living patients; the results were poor in the remaining nineteen, though three have subsequently improved following thoracoplasty. The authors conclude that unless with the further lapse of time the final result is not good the procedure should continue to be a useful collapse procedure.

Bacterial Endarteritis Complicating Patent Ductus Arteriosus.—Touroff and Vesell report four cases of subacute bacterial endarteritis complicating patent ductus arteriosus treated surgically. The rationale of the treatment is that ligation or excision often controls the bacteremia. For successful surgical eradication of the infection the vegetations should be confined to the ductus, and the ductus should be of sufficient length to permit excision. Unfortunately it is impossible to determine whether the vegetations are confined to the ductus, but certain information is available for the latter requirement. In the reported cases of operative uninfected patent ductus the length of the ductus varied from 0.5 to 1.2 cm. Practically all these operations were performed on children. It may be assumed that in adults the ductus would be larger. In three of the authors' cases the structure appeared to be of sufficient length to be divided and doubly ligated. If at operation the ductus is found too short the question arises whether operation is contraindicated. In the authors' first case the ductus was not completely excised but was divided and ligated as close to both orifices as possible. The interiors of the pulmonary artery and aorta were not inspected and the location of the vegetations was not known. The patient recovered from the infection following operation. This means that the vegetations were confined to the ductus and were completely excluded from the circulation by operation, or that they were also present in the pulmonary artery but healed quickly following closure of the arteriovenous shunt. If the latter were the case it appears that such spread would not contraindicate operation. If vegetations extend into the left side of the heart or the aorta, operation appears inadvisable as foci in these regions would continue to feed organisms into the peripheral circulation despite excision, division or ligation of the ductus. In the second case this was the sequence of events; therefore every effort should be made to determine involvement of the left side of the heart and aorta preoperatively. As subacute bacterial endarteritis superimposed on patent ductus is almost invariably fatal it appears justifiable to maintain that, barring the presence of major coexisting congenital cardiac anomalies or the generally poor condition of the patient, operation is contraindicated only in cases in which left-sided cardiac or aortic vegetations are present. The first of the authors' four adults recovered and has been well since operation nineteen weeks ago. The second patient was temporarily improved but the bacteremia persists seventeen weeks after operation. The third and fourth patients died of uncontrollable hemorrhage during operation. The recovery of one of the four patients affords little indication of the results regularly anticipated from such treatment, but since surgical therapy was successful in this case it should encourage others to give the method a thorough trial in the hope of reducing the mortality rate, which even the most optimistic observers place between 95 and 97 per cent.

Lobectomy and Pneumonectomy in Pulmonary Tuberculosis.—Dolley and Jones report seven cases of pulmonary tuberculosis, in four of which pneumonectomy and in three lobectomy was done. They advocate: (1) preliminary thoracoplasty with extrapleural apicolysis (while occasionally the final thoracoplastic stage may be included with the lobe or lung removal, they feel that this combined operation is usually inadvisable), (2) serial dissection of the hilar structures if technically possible, (3) the usual care in closure and burial of the bronchus, (4) immediate open drainage of the pleural cavity which by virtue of extensive thoracoplasty has become scarcely more than a broad slit, (5) painstaking removal by catheter suction of all possible infected material from the respiratory tract, (6) constant insistence during the early postoperative hours that the patient, with his pain controlled by analgesics, cough effectively and (7) minimal manipulation and instrumentation of the affected lobe or lobes preventing the purulent material within from

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soiling the neighboring or contralateral pulmonary subdivisions. They believe that if, following thoracoplasty, it becomes apparent that a given patient is to remain disabled and his general condition warrants the surgical hazard and the technical difficulties are not too great, an attempt to remove the lobes involved is indicated. When bronchial stenosis is extreme or thick-walled cavities and extensive bronchiectasis exist which cannot be cared for adequately by extensive collapse or local compression this final measure is not justified until it is certain that nothing less radical will succeed. The final decision for lung removal is made after it has been found that extensive thoracoplasty is insufficient. Thoracoplasty is the preliminary procedure of choice. The authors are convinced that the removal of tuberculous lobes will become a reasonably safe and comparatively common procedure within the next few years. If the operative risks attain reasonable balance, lobectomy will be preferable to extensively necrotic lobe collapse. Contralateral spread is the most potential enemy at present. However, more and more potent weapons are being developed to combat it. Lobectomy should be limited at present to those patients for whom there is no other satisfactory recourse, and then only when the mediastinum and the chest wall have been stabilized and the residual potential empyema space has been minimized. Of their four patients undergoing pneumonectomy, two are dead and two will probably never regain their health. All had early or late contralateral spread. From the results in these patients the authors conclude that such patients should be prepared for pneumonectomy by thoracoplasty as more often than not the general condition of the patient is improved by thoracoplasty. Of the three patients on whom lobectomies of the right upper lobes were performed, two are well and able to work. The general condition of the third is excellent although her last sputum was positive. Toxic fatigue is notably absent in these patients, for their tuberculosis is gone with their lobes. In two, thoracoplasty preceded lobectomy; the postoperative course of all three was uncomplicated and in none was there a spread.

Laryngoscope, St. Louis 50:797-920 (Sept.) 1940

- Otogenic Complications; Résumé and Discussion of Literature for 1939. L. G. Richards, Boston.—p. 797.
Observations on Conservation of Hearing. H. Newhart, Minneapolis.—p. 847.
The General Problem of Deafness in the Population. W. C. Beasley, Bethesda, Md.—p. 856.
Otic Hydrocephalus: Report of Two Cases. J. J. Gitt, St. Louis.—p. 906.

Minnesota Medicine, St. Paul 23:681-754 (Oct.) 1940

- An American Health Program. N. B. Van Etten, New York.—p. 681.
Roentgenologic Diagnosis of Intraspinous Protrusion of Intervertebral Disks. J. D. Camp, Rochester.—p. 688.
Treatment of Protruded Intervertebral Disks. J. G. Love, Rochester.—p. 692.
Intracranial Tumors: Study of 467 Histologically Verified Cases. A. B. Baker, Minneapolis.—p. 696.
Small Carcinomatous Gastric Lesions Simulating Chronic Benign Ulcer: Present Status of Differential Diagnosis and Treatment. G. B. Eusterman, Rochester.—p. 703.
Surgical Treatment of Gastric Cancer Masquerading as Benign Disease. W. Walters and W. H. Cleveland, Rochester.—p. 709.
Indications for Use of Iron in Treatment of Anemias. P. F. Eckman, Duluth.—p. 712.
Toxic Effects of Carbon Tetrachloride: Report of Case. W. S. Hagen, H. A. Alexander and T. A. Peppard, Minneapolis.—p. 715.
- Surgical Treatment of Gastric Cancer Masquerading as Benign.**—Walters and Cleveland believe that too often gastric and duodenal ulcers are grouped under the misleading title of "peptic ulcer" and their inherent dissimilarities neglected and thus not recognized as occurring in individual types of tissue in which pathologic reaction and response to medical and surgical treatment is different. A large chronic gastric ulcer (more than 2.5 cm. in diameter) in a patient more than 40 years of age, especially if perforation, obstruction or hemorrhage has been present, or one on the greater curvature or near the pylorus usually should be removed surgically without delay, as few of these lesions respond to medical treatment and many may be carcinomatous. The small gastric ulcer which has failed to heal or has recurred under adequate medical management should be

Missouri State Medical Assn. Journal, St. Louis 37:409-454 (Oct.) 1940

- Studies in Blood Coagulation Disturbances. H. N. Sanford, Chicago.—p. 409.
Functional Menstrual Disturbances. E. D. Plass, Iowa City.—p. 418.
Circulatory Mechanism Disorders: Recognition and Management of the Commoner Sudden Disturbances. G. Herrmann, Galveston, Texas.—p. 421.
Food Allergy. H. J. Rinkel, Kansas City.—p. 428.
The St. Louis Pneumonia Control Program: Statistical Evaluation of Various Forms of Therapy. E. Sigoloff, St. Louis.—p. 431.
Id.: Epidemiologic Aspects. S. E. Sulkin, St. Louis.—p. 435.
Twenty-Eight Years with Ether. O. O. Smith, St. Louis.—p. 440.
Premarital Examination Laws. L. D. Cady, St. Louis.—p. 443.

Review of Gastroenterology, New York 7:373-456 (Sept.-Oct.) 1940

- Effect of Parathyroid Hormone and of Activated Ergosterol on Gastric Secretion in Dog. B. P. Babkin, Montreal.—p. 373.
Plea for More Frequent Use of Duodenal Alimentation in Treatment of Peptic Ulcers. M. Einhorn, W. H. Stewart, F. Huber and C. W. Breimer, New York.—p. 383.
Symptoms, Diagnosis and Treatment of Chronic Cardiospasm. E. B. Freeman, Baltimore.—p. 385.
Early Diagnosis of Gastric Cancer. S. Cytronberg, Mexico City, Mexico.—p. 391.
Standardized Measures for Study of Cecum, Special Reference to Undescended Cecum. A. X. Rossien, Kew Gardens, N. Y., and A. J. Cantor, Flushing, N. Y.—p. 399.
Indications and Contraindications of Medical Treatment in Cholecystitis and Duodenal Ulcer. T. Miller, Dallas, Texas.—p. 403.
Indication for Operation in Acute Cholecystitis. J. L. Ransohoff and H. Topolofsky, Cincinnati.—p. 412.
Surgical Treatment of Gallbladder Disease. R. Zollinger, Boston.—p. 420.
Secretin Test as Aid in Differential Diagnosis of Steatorrhea: Report of Fourteen Cases. J. S. Diamond, S. A. Siegel and S. Myerson, New York.—p. 429.

West Virginia Medical Journal, Charleston 36:441-488 (Oct.) 1940

- Acute Surgical Lesions of Abdomen. I. Abell, Louisville, Ky.—p. 441.
Management of Urinary Infections in Children. R. M. Tyson, Philadelphia.—p. 451.
Androgens in Medicine. L. C. McGee, Elkins.—p. 458.
Diverticulum of Female Urethra with Calculi: Case Report. G. G. Irwin, Charleston.—p. 470.
Aortic Aneurysm: Case Report. A. C. Woofter and O. B. Barker, Parkersburg.—p. 472.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:437-478 (Oct. 5) 1940

- The Journal and the Profession: Some Memories. D. Power.—p. 437.
*Cerebrospinal Fever: Analysis of 124 Cases. R. W. Cushing.—p. 439.
Examination of the Heart in Recruits. G. Bourne.—p. 442.
Colorimetric Standards for Emergency Estimations of Certain Constituents of Blood and Cerebrospinal Fluid. E. J. King.—p. 445.
Recent Advances in Treatment of Gonorrhea. D. J. Mackinnon.—p. 448.

Cerebrospinal Fever.—Cushing states that from Nov. 11, 1939, to May 26, 1940, 124 patients with cerebrospinal fever differing from that seen in 1914 to 1918 were admitted to the Military Isolation Hospital, Aldershot, and treated with benzylsulfanilamide derivative by the intravenous route. The onset of the fever was sudden. Many patients went to bed feeling quite well and awoke in the morning with intense headache, frequently accompanied by vomiting. Incubation appeared to be from twenty-four to forty-eight hours. Some patients had various symptoms, especially sore throat or general malaise lasting one to seven days before the appearance of the headache. The fulminating septicemic type was even more sudden than this. Twenty-eight of the cases were classified as slight, 49 as moderate, 41 as severe and 6 as fulminating septicemic. The clinical picture was that of an extremely ill patient with the anxious expression of one in distressing pain. The lips and cheeks were pale and gray, showing a definite toxemia with much blood destruction. The skin was damp with perspiration. The most characteristic and distressing symptom was the intense and intolerable headache. The removal of from 30 to 50 cc. of cerebrospinal fluid would relieve the distressed condition immediately. The next important sign (in 116 cases) was nuchal rigidity with intense pain on attempting to approximate the chin to the chest. Vomiting was fairly constant and lasted from one to four days. During this stage benzylsulfanilamide derivative was valuable. Often the patient's mental condition was abnormal, presenting considerable cerebral irritation and mental depression. The temperature was no guide in establishing a prognosis or determining the severity of the case. Only 3 patients had a temperature of 103 F. on admission; 102 had less than 100 F. The pulse rate was much more indicative of the severity of the infection. A slow pulse rate was evident only in cases of increased pressure of the cerebrospinal fluid or in full dosage of the sulfonamide drug used. The reflexes followed no definite pattern. The patients with the fulminating type of fever showed meningeal signs; but the predominant clinical picture was acute generalized toxemia, and some were presumably septicemic in nature. In others the clinical picture simulated typhoid with pyrexia and a macular rash and in these cases the meningococcus could be isolated by blood culture. Within twenty-four or even twelve hours after the initial intravenous injection of benzylsulfanilamide derivative and lumbar puncture the temperature fell to normal, the intensity of the headache was diminished and in some cases entirely eliminated, nuchal rigidity lessened and vomiting ceased or lessened in persistence and severity. By this time sulfapyridine given orally in diminishing amounts caused no vomiting. Treatment was stopped in eight or nine days and the patient proceeded to uneventful recovery, was allowed up in from thirteen to twenty-one days and after four or five weeks of hospital treatment was discharged on five weeks' convalescent leave. After five weeks of convalescence 25 patients declared themselves perfectly well and fit, 48 complained of early fatigue on exercise and occasional dizziness, 6 complained of pain in the back and 42 exhibited effort syndrome in varying degrees of severity. Forty-eight were recommended for a period of light duty under the supervision of a regimental medical officer and 25 were returned to their unit as "fit for duty." For the others further convalescent treatment was recommended before their return to supervised light duty. The majority of the patients were young militiamen who contracted the infection after a short period of service. There were four deaths. Since May there have been eleven more admissions, and as no other deaths have

occurred the total mortality rate is brought down to 2.9 per cent. Benzylsulfanilamide, 20 cc. of a 5 or 10 cc. of a 10 per cent solution, is injected intravenously into one of the veins over the antecubital fossa. This can be repeated in four to eight hours, according to the severity of the case, and may be continued for three or four days until the patient's initial signs and symptoms disappear. The results were so constantly good and the effects so speedy that the drug is recommended for routine treatment at the outset in all cases except perhaps the mildest. Once the diagnosis is made, no further lumbar punctures are performed unless signs of intracranial pressure arise.

Quarterly Journal of Medicine, Oxford

9:193-246 (July) 1940

- Poisoning by Methyl Mercury Compounds. D. Hunter, R. R. Bomford and Dorothy S. Russell.—p. 193.
*Liver Function in Thyrotoxicosis. N. F. MacLagan and F. F. Rundle, with experimental data by H. B. Collard, F. H. Mills and F. F. Rundle.—p. 215.
*Action of Parasympathetic-Mimetic Drugs in Asthma. H. H. Moll.—p. 229.

Liver Function in Thyrotoxicosis.—MacLagan and his colleagues determined the hepatic function of forty-one patients with hyperthyroidism by means of a modified galactose tolerance test. Thirty of the patients showed definite impairment of hepatic function, and the remaining eleven gave results in the upper normal range (galactose index above 68). Clinical grading of the cases as severe, moderate and mild showed a definite relationship between the galactose index and the severity of the disorder. A significant correlation existed between the galactose index and the basal metabolic rate of untreated patients. Rest and iodine therapy had little effect on the galactose index, but in most instances thyroidectomy produced a prompt fall to normal values. Some residual impairment was demonstrated in a few cases studied at long intervals after thyroidectomy for severe hyperthyroidism. Daily subcutaneous administration of thyroxine to rabbits for periods up to seventeen days produced a marked impairment of tolerance to galactose injected intravenously. The livers of these animals also showed severe focal necrosis when examined microscopically. The galactose tolerance depends essentially on hepatic glycogenesis and this is the hepatic function which is particularly impaired in thyrotoxicosis and therefore the test reveals the typical disorder of the liver in this disease. It is possible that the toxic effect of the thyroid hormone on the liver is connected with its action in interfering with glycogenesis. The authors' data suggest that, when the galactose index is markedly high, structural hepatic damage is probably present. When the galactose index is only moderately raised their data do not show whether the change is a functional one or whether organic lesions are also present. The fact that normal limits were usually regained in fourteen days favors the functional explanation, and the fact that the iodine therapy has little or no effect suggests an organic cause. The galactose index provides an additional physical sign of hyperthyroidism.

Action of Parasympathetic-Mimetic Drugs in Asthma.—Moll observed the effect of mecholyl (acetyl-beta-methylcholine chloride) on twenty-eight persons with asthma and thirty-eight control subjects (normal medical students and non-asthmatic hospital patients with or without other types of respiratory disorders). He finds that the mecholyl test does not help to differentiate the different types of asthma, and patients with reflex asthma or persons in whom attacks are released psychogenically through nervous channels are not more susceptible to mecholyl than persons with infective or allergic asthma. However, the test may be helpful in the diagnosis between true asthma and respiratory neurosis, and especially hysterical hyperpnea: bronchospasm occurs in the former instance but not in the latter. The twenty-eight asthmatic subjects almost invariably responded with respiratory symptoms, which varied in intensity from slight wheeziness to severe asthma-like attacks. The control subjects showed general signs of parasympathetic stimulation (flushing, sweating, lacrimation and salivation) but chest symptoms did not develop. The tropism of choline derivatives for the bronchial system appears to be due not to a state of increased sensitivity of

the whole of the parasympathetic system (vagotonia) but only of the bronchial nerve endings or of the bronchial muscle itself. Pulmonary damage is an essential factor in determining the abnormal bronchial response. No matter how mild or infrequent the attacks of asthma may be, an asthmatic subject is nearly always susceptible to the drug. The asthma-like attack produced by choline derivatives is similar to, but probably not identical with, spontaneous asthma.

Schweizerische medizinische Wochenschrift, Basel

70:849-872 (Sept. 7) 1940. Partial Index

*Symptom of Narrowed Intervertebral Disk. H. Schaer.—p. 849.

*Primary Inoculation Tuberculosis of Vulva Caused by Cohabitation. M. Schmid.—p. 852.

Symptomatology and Therapy of Thyrogenic Migraine. E. I. Steuer.—p. 853.

Narrowed Intervertebral Disk.—Schaer directs attention to the fact that narrowing of the intervertebral disk is frequently encountered in diseases of the vertebral column. It is observed as an accompanying symptom of numerous degenerative changes of the intervertebral disk or of the adjoining vertebral bodies in the frequent spondylosis deformans. It is seen as a characteristic sign in juvenile kyphosis, in kyphosis of the aged and in osteoporosis of the aged. In all these cases the narrowing involves all or several of the disks. The narrowing of an isolated intervertebral disk occurs much less frequently and is difficult to diagnose. The author describes several cases in which this symptom was present and discusses the underlying pathologic process. Isolated narrowing of an intervertebral disk is due either to a reduction in its volume as the result of primary degeneration of the disk itself (osteochondrosis) or to pathologic processes in the surrounding tissues. The narrowing is found chiefly as an early roentgenologic symptom of tuberculous spondylitis. It is the result of the breaking through of the still intact intervertebral disk into a circumscribed diseased area of the adjoining vertebra. The deformation resulting from this breaking through leads to a seeming contraction, which at times is regular and at others irregular and which is frequently accompanied by a dorsal displacement of the vertebra above it. This early symptom of tuberculous spondylitis corresponds to the anatomic stage of the cavernous destruction of the vertebral body, a fact that has to be considered in estimating the age of a tuberculous process in the vertebral column.

Primary Inoculation Tuberculosis of Vulva.—Schmid maintains that in order to designate an extrapulmonary tuberculosis as a primary complex it is necessary to demonstrate the characteristics of the primary complex, namely a tuberculous inflammatory lesion at the portal of entry with swelling and caseation of the regional lymph nodes, and to rule out the existence of a tuberculous process in other parts of the body. The literature on primary extrapulmonary tuberculosis contains cases developing from ritual circumcision, from the injection of incompletely sterilized milk, from the piercing of ear lobes for the attachment of earrings, from injuries of the feet while walking barefoot, from contact with tuberculous cattle (in veterinaries and butchers) and from the kiss of patients with pulmonary tuberculosis. The possibility of a primary tuberculosis caused by cohabitation was demonstrated in guinea pigs in 1920. Five human cases of primary inoculation tuberculosis by cohabitation have been reported since 1929. The author reviews these cases and presents a detailed report of a case of his own. A woman aged 28 developed an ulcer at the attachment of the hymen a short time after defloration. Later the inguinal glands became sensitive to pressure. The diagnosis was undecided between syphilis, venereal lymphogranuloma and simple defloration ulcer. Repeated Wassermann and Frei tests were negative. Examination for gonorrhea was likewise negative. Some time later one of the inguinal glands perforated spontaneously, but the pus exuding from this gland contained no bacteria. Later several lymph nodes were excised and the microscopic examination disclosed caseous tuberculosis. Under a strengthening regimen, tuberculin therapy and local roentgen irradiation the lymph nodes decreased in size, the general condition improved and the vulval ulcer healed. Pirquet's tuberculin reaction was still strongly positive at the time of the

patient's dismissal from the hospital. The primary tuberculous complex on the vulva induced an examination of the cohabitation partner. This revealed tuberculosis of the prostate and of the seminal vesicles in a man who previously had been treated for tuberculosis of the bones.

Archivos de Oftalmología de Buenos Aires

15:377-428 (Aug.) 1940. Partial Index

Encephalography in Diagnosis of Chiasmal and Hypophysial Lesions. M. Balado and M. F. Oribe.—p. 377.

*Sulfanilamide in Trachoma. J. Lijo Pavia.—p. 400.

Sulfanilamide in Trachoma.—Lijo Pavia, head of the Argentine committee for the prevention of blindness, reports on sulfanilamide treatment of trachoma of three groups of twenty-six patients each. These groups included children and adults. The disease was of the first, second and third degrees. The patients were not hospitalized; they remained at home in order not to be exposed to the sun's rays. The drug (azosulfamide) was administered on fifteen consecutive days in a daily dose of 0.02 Gm. for each kilogram of body weight for the first five days, 0.03 Gm. for the next five days and 0.04 Gm. for the last five days. The treatment was well tolerated. Photophobia, lacrimation, blepharospasm and conjunctival hyperemia showed improvement within the first five days of the treatment and generally disappeared in the course of it. Edema was reabsorbed, the pannus cleared and the transparency of the cornea and vision improved. The nodules became smaller and in some cases disappeared in the course of treatment or sometime after. Six patients were observed for three months after discontinuation of the treatment. Some of the patients instilled a drop of a 0.5 per cent zinc solution or an eyewash of a weak solution of mercuric oxycyanide. All the nodules had diminished in number and size and in some instances had disappeared. The author believes that sulfanilamide has an immediate therapeutic action on trachoma and a late action on the remaining nodules, with the probable exception of cases in which there are advanced forms of the disease. The patients had the treatment too recently to enable one to predict the future behavior of the disease and whether or not the results will be permanent.

Nordisk Medicin, Gothenburg

7:1303-1336 (Aug. 3) 1940

Roentgen Diagnosis in Acute Abdominal Cases. G. Petré.—p. 1303.

*Hemorrhagic Disease in Newborn: Hypoprothrombinemia in Newborn. L. Salomonsen.—p. 1309.

Hypoprothrombinemia of Newborn.—Salomonsen states that all hemorrhagic conditions of the newborn are accompanied by a delayed coagulation time which depends on a hypoprothrombinemia due to vitamin K deficiency probably originating because of deficient formation of vitamin K in the sterile intestinal canal of the newborn. He asserts that giving a little cow's milk as early as from the second hour of life will almost wholly prevent this physiologic disturbance in coagulation.

Hospitalstidende

*Two Cases of Constitutional Infantile Anemia. P. Hjorth.—p. 1313.
Animal Experimentation on Heat Treatment of Malignant Tumors. K. Overgaard and H. Okkels.—p. 1317.

Constitutional Infantile Anemia.—Hjorth presents the cases of a brother and a sister, in both of whom, at the age of 8, a grave hyperchromatic anemia developed in the course of a few months with leukopenia and thrombopenia and hemorrhagic diathesis. There was hypoplasia, but not aplasia, of the bone marrow, also hypoplasia of the thymus and, in the boy, hypoplasia of the testes. Congenital bone deformities were present, clubfoot in the boy, bilateral luxation of the hip in the girl. The children were kept alive for two and a half years and four years respectively by means of blood transfusions, thirty in each case; no other treatment was of avail. A marked disposition to congenital bone deformities was established in the mother's family, and one member of the father's family was born without thumbs. These cases resemble five cases reported in the literature (Fanconi, Uehlinger and van Leewen) and designated by Uehlinger and van Leewen as "congenital infantile anemia."

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THE UNIVERSALITY OF DIABETES

A SURVEY OF DIABETIC MORBIDITY IN ARIZONA

THE FRANK BILLINGS LECTURE

ELLIOTT P. JOSLIN, M.D.

BOSTON

WITH THE COOPERATION OF THE PHYSICIANS
IN ARIZONA

I believe that the incidence of diabetes should be highest in communities in which (1) the average age is greatest, (2) women predominate, (3) obesity is most frequent, (4) the proportion of Jews is greatest, (5) medical supervision is closest and (6) deaths are most accurately reported. Therefore I am puzzled to explain why the mortality from diabetes should be nearly twice as high in the United States as in Canada, when the two countries are separated only by an arbitrary line. Why should the incidence of diabetes double in the United States in the ten years 1880 to 1890 and then take thirty years to do so again—between 1900 and 1930? Why should it double in Italy and Switzerland between 1920 and 1934? Why should the death rate from diabetes in Rhode Island in 1937 be four times that in Arizona or, to make the question more general, why should the rate for Alabama, Arizona, Arkansas and New Mexico be the lowest in the country in 1937, 10 or less per hundred thousand, and that for Rhode Island, New York, Massachusetts and Connecticut be the highest, or more than 33 per hundred thousand?

Such thoughts were coursing through my mind when I received the flattering invitation of the executive committee of the Section on Practice of Medicine of the American Medical Association to deliver the Frank Billings Lecture.

An armchair statistical study of the incidence of diabetes does not appeal to me; field work does. Already there are available two excellent examples of the latter—the survey conducted in Massachusetts under the direction of Bigelow and Lombard¹ of the state board of health in 1929-1931 and that in Washington sponsored by the National Institute of Health² in 1935-1936.

These surveys, however, were concerned with the frequency of diabetes in areas in which its statistical mortality was reported to be highest. This left to me the opportunity to undertake field work in areas in which the incidence of diabetic mortality was reported to be the lowest. I reasoned that only good could come

from such a survey, because if the low incidence proved to be correct one could concentrate on a study of the cause for this immunity and might even encourage hereditarily predisposed diabetic patients to migrate to such a region. Contrariwise, if the survey showed that the information was ill founded, new cases of diabetes automatically would have been disclosed and brought under treatment, lives have been spared or prolonged and the diabetic army in the United States expanded. Moreover, of still greater consequence would be the outcome, if the evidence was frankly decisive and the reported low mortality completely overthrown, because it would put a question mark before every town, city, state or, indeed, country in the world which reported an extraordinarily low death rate from diabetes.

Where should such a survey be carried on? Obviously in one of those localities in which the reported mortality from the disease was the lowest, and in 1937 the four states were Alabama, Arkansas, Arizona and New Mexico. Alabama and Arkansas were at once ruled out by me because those states are too populous and they have too many doctors to make intimate contact possible. Arizona appeared preferable to New Mexico for the purpose because during the month of February it is said to be more available for investigation, and because Arizona is particularly diversified in climate, altitude and composition of its population.

Arizona having been chosen, the problem to be solved was why Arizona had a diabetic mortality of 10 per hundred thousand and Rhode Island one of 42 per hundred thousand in 1937, with three other states in the East—New York, Massachusetts and Connecticut—having diabetic mortalities more than 33 per hundred thousand. These mortalities were evidently not chance mortalities for a single year. This is shown in table 1, in which average mortalities are given for 1934 to 1938 of the states with the four highest and the four lowest rates. Here it will be seen that the higher rates range between 31 and 37 and the lower rates between 9 and 11 per hundred thousand of population, whereas the United States showed an average rate of 23.

While considering the possibility of making the survey, I sought advice and received it wholeheartedly from Dr. Herbert L. Lombard of the Massachusetts State Board of Health, who encouraged and, indeed, urged me to carry it on. I also received assistance in many ways from the Surgeon General of the Public Health Service, Dr. Thomas Parran, and from Dr. Louis I. Dublin and Mr. Herbert H. Marks of the statistical department of the Metropolitan Life Insurance Company and, finally, most valuable counsel from the editor of THE JOURNAL.

Certain contrasts between Arizona and Rhode Island first deserve mention because of their importance in explaining the wide differences in diabetic mortality. The area of Arizona is 113,810 square miles and more

Read before the Section on Practice of Medicine at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Bigelow, G. H., and Lombard, H. L.: Cancer and Other Chronic Diseases in Massachusetts, Boston, Houghton Mifflin Company, 1933.

2. The Magnitude of the Chronic Disease Problem in the United States, Washington, D. C., Division of Public Health Methods, National Institute of Health, U. S. Treasury Department, Public Health Service, 1938.

DIABETES SURVEY—JOSLIN

JOUR. A. M. A.
Dec. 14, 1940

than 100 times that of Rhode Island, which is 1,067 square miles. In Arizona much of the land is made up of reservations for the Indians, forests, parks and mountainous regions save those penetrated by main highways, and this makes communication difficult. In 1937 the estimated population of Arizona was 409,000 and that of Rhode Island 681,000. The density of population per square mile is 3.8 in Arizona and 644 in Rhode Island. The relative number of physicians to

TABLE 1.—States with Highest and Lowest Diabetes Mortality Rates per Hundred Thousand in 1937 and 1934-1938

	Highest			Lowest	
	1937	1934-1938		1937	1934-1938
Rhode Island.....	42.0	36.9	Alabama.....	10.6	11.0
New York.....	36.9	36.9	Arizona.....	10.0	9.8
Massachusetts.....	33.7	34.8	Arkansas.....	9.2	8.5
Connecticut.....	32.5	31.5	New Mexico.....	8.1	8.6
New Hampshire.....	32.9			

the population differs less than one might conceive, one to 772 in Arizona and one to 726 in Rhode Island, although in the urban areas in Arizona there are 27.6 physicians per 10,000 inhabitants and only 5.4 in the rural sections of the state. The population in Arizona in towns and villages less than 2,500 constitutes two thirds of the total inhabitants, but in the latter state it is hardly fair to class the population of many of the small towns as distinctly rural. The distance across Arizona from north to south is nearly 400 miles and from east to west 340 miles, as compared with 48 and 37 miles respectively for Rhode Island. How large a share possibilities for the medical supervision of the population count for the divergence in mortality of diabetes in the two states no one knows. Certainly it must be a factor, but in this discussion no percentage estimation of the part medical supervision plays will be adduced.

CRUDE VERSUS ADJUSTED MORTALITIES FOR AGE AND SEX

Diabetes is a disease in which the influence of the age and sex of the population is profound. These are well recognized facts. Table 2, compiled from data published by the National Health Board in its survey of 2,502,391 persons living largely in urban areas, enables one to see at a glance how misleading comparisons can be if based on crude statistical data alone. Thus only one diabetic individual can be found among 2,500 boys and girls and another among 1,700 young adults between the ages of 15 and 24 years. At these ages sex is indifferent, but above this level women predominate. At the age of 65 years one man in seventy has the disease and one woman in sixty. In Massachusetts over the age of 45 there is 1.1 female for every male. In Arizona the comparable figure is 0.73. Thus the simple adjustment by age and sex of the population in Arizona and Rhode Island resulted in the year 1937 from one to four to one to three, and, for the years 1929 to 1931 the crude ratio of one to three and five-tenths when adjusted to the census of 1930 falls to one to two. These standard compilations, therefore, made the task of explaining the difference in mortality less formidable, because with this aid half of the hurdles are passed.

CONTRIBUTORY CAUSES OF DEATH IN ARIZONA AND MASSACHUSETTS

The large number of deaths from tuberculosis in Arizona, 802 in 1939, compared with fifty-seven from diabetes furnished a chance opportunity to explain its statistically low diabetic mortality. Tuberculosis takes precedence over diabetes. If it could be demonstrated that as many patients with tuberculosis had diabetes in Arizona as in Massachusetts there would be a great accession in diabetic mortality data. In order to determine this, copies of Arizona death certificates bearing the diagnosis tuberculosis were made, and these were analyzed under the supervision of Dr. Lombard, but the results indicated only a fraction as many cases of diabetes among the tuberculous in Arizona and in fact all other groups in which diabetes occurred as a secondary cause, as in Massachusetts. For combined contributory causes the figure for Massachusetts was 11.3 per cent and for Arizona only 1.4 per cent. Such a striking difference suggests that in Arizona diabetes as a secondary cause of death frequently is omitted from the death certificate.

FIELD WORK

Statistical computations have changed the difference in ratio of diabetic mortality between Arizona and Rhode Island from one to four to one to two. To turn now to diabetic field work, the plan of campaign adopted was a direct outgrowth of a phrase, "the fecundity of the aggregation," once used and elaborated on in an informal evening discussion in his home, and later published, by Prof. Josiah Royce of Harvard.³ By it he meant that, when people get together and discuss things, something new and better is likely to arise than from one of the individual members of the group, uppermost in my mind was how I could secure this "fecundity of the aggregation" in Arizona. That was quickly solved, because first of all the Arizona Board of Health put its office, its staff, its publication and its good will at my disposal, and this action was quickly followed by that of the Arizona State Medical Society. In addition, I was given the help of the Veterans' Bureau facilities and Indian bureaus, and every particle of red tape was cut. Not only did the press of Arizona speak favorably

TABLE 2.—Ratio of Diabetes in the Population

Age	Males	Females
0-14.....	1:2,500	1:2,500
15-24.....	1:1,700	1:1,700
25-34.....	1:1,100	1:1,100
35-44.....	1:500	1:900
45-54.....	1:225	1:300
55-64.....	1:100	1:125
65 and over.....	1:70	1:50

These data, adapted from the National Health Survey, are based on 9,182 diabetic patients in a surveyed (urban) population of 2,502,391 persons.

of the study but their medical editor put in newspaper form the crude talks on diabetes which I had labored to devise and, finally, the pharmaceutical association of the state reduced the price of the solution used for the Benedict test for two months so that there would be no excuse for doctor or layman to be deprived of an examination of the urine. The Phoenix Pathological Laboratory reduced its fees for blood sugar tests to a wholesale minimum.

With all these agencies aiding and abetting the diabetic survey, I sent airmail letters to each doctor in

3. Royce, Josiah: Science 39: 551, 1914.

the state asking him if he would report by name or initial the diabetic patients under his care, and I confess also to the effrontery of asking him to tell me whether he himself had diabetes. The airmail letters were supplemented by two trips to Arizona and a three weeks stay in the state during which I traveled from Yuma to Ganado, from Douglas to Flagstaff; in fact, I visited all communities in the state with a population of more than 3,000 save two, and many of the smaller towns.

TABLE 3.—*Arizona and Rhode Island Populations per Square Mile and Crude and Adjusted Diabetic Mortalities, 1937 and 1930-1938*

1937	Popu- lation per Square Mile	Physi- cians to Popu- lation	Diabetic Mortality per 100,000			
			1937		1930-1938	
			Crude	Adjusted	Crude	Adjusted
Arizona.....	3.8	1:772	10.0	13	8.8	10.1
Rhode Island....	644.0	1:726	42.0	37	28.3	22.4

The doctors I met were extraordinarily kind. Often they welcomed me at dinner or at luncheon, perhaps in a hospital where I had an excellent opportunity to meet them individually, and when I wished to travel from one locality to another they would transmit me at a speed of 75 miles an hour, more or less, thus eliminating distance and taking advantage of Providence, R. I., with its speed limit of 25 miles an hour. Besides these more formal meetings I rang doorbells like any detail man and, when an elderly doctor was doubtful about his having or not having diabetes, got his specimen then and there.

In reporting the results of the canvass for diabetes in Arizona I will begin with that of small and special groups, because each yields its lesson. These groups are of especial value for comparison with similar ones elsewhere. The first is a microcosm.

Jews.—In Arizona Jews number about 2,000 (1,755 in 1937). They constitute less than one two-hundredth of the population, but when I counted Jews among all the diabetic patients reported by the doctors of the state they numbered eighteen, or about one fortieth of the total number of diabetic patients, or proportionately four or five times as many. Thus the Jewish racial incidence in Arizona is even stronger than that in Boston, where years ago there were two and one-half diabetic Jews for one diabetic Gentile, a figure based on larger numbers and, in my opinion, nearer to the truth.⁴ If the 100,000 \pm Mexicans now in Arizona, representing one fourth of the total population, were replaced by Jews, who show four times the total diabetic morbidity incidence, the figure for diabetic morbidity in Arizona would just about double the incidence I got for the whole state.

I sense your criticism that the Jews, like so many others of Arizona's population, are newcomers and do not fairly represent the original population of Arizona, but to this I would answer that there is very little indigenous population in that state. At a dinner of twenty-three physicians in Tucson, when I asked how many of those present were born in the state not one hand was raised. However, I grant the validity of such objections. Indeed, the opportunity to meet them was one of the reasons which led me to select Arizona as a test state for diabetes, because it has some 40,000 to 50,000 original inhabitants, namely the Indians.

In this field work among the Indians not one particle of credit is due to me. All is due to the physicians

in the Indian service, who cooperated in every way possible. I cannot say enough for that service, and I know whereof I speak, because I visited Indian hospitals in Sacaton, Ganado, Fort Lewis, San Carlos and the Indian school and Indian hospital in Phoenix. By no means did I canvass all the Indians or go to all the reservations with their varied institutions, but I can say emphatically that I had most cordial responses from the Indian Bureau in Washington, its representatives in the West and individually from all the government agencies, and what I say of the Indian service I can say also of the assistance I received from the two United States Veteran Facility hospitals in Tucson and Fort Whipple. Moreover, I should also mention the cooperation of the members of the staffs of the various hospitals in mining centers, Bisbee, Jerome and Globe, who took the pains to make it possible for me to meet and question physicians living nearby, although not on their own staffs.

The high grade of medical care afforded Indians in Arizona by the United States government is not sufficiently known, even among the physicians of Arizona. I cannot praise it too strongly not only for what it is doing now but for what I know has been arranged for it to do in the immediate future.

Indians.—From Washington I learned that two Indians yearly (actually eleven Indians for the six years 1934 to 1939) were reported to have died with diabetes. In addition, among 6,331 admissions (90 \pm per cent Indians) between the years 1931 and 1936 to the Sage Memorial Hospital at Ganado,⁵ a private institution on the Navajo reservation, the existence of diabetes was demonstrated in one Indian. When the final count of the cards with the names of the diabetic Indians living in Arizona was made I had seventy-one, and the statistical conscience of the statistical department of the Metropolitan Life Insurance Company, which revised my data, forced me to add two more, allocating these to Indians from the total number of cases with nationality unclassified, thus making seventy-three in all.

It is not strange that so few diabetic Indians were admitted to the Sage Memorial Hospital. Their patients are young. Among 1,429 admissions during 1939, only seventy-five were past the age of 50. The age distribution is given in table 4.

The survey certainly did not include all the Indians in the state. I should think it doubtful that it included

TABLE 4.—*Age Distribution of Patients Admitted to Sage Memorial Hospital in 1939*

Under 5 years.....	375	20 to 35 years.....	417
5 to 12 years.....	180	35 to 50 years.....	145
12 to 14 years.....	44	50 to 65 years.....	45
14 to 20 years.....	193	Over 65 years.....	30

more than two thirds as a maximum and more likely only one half. Granting, however, that there was not an Indian in the state escaping the survey, and comparing the seventy-three live diabetic Indians with the two reported dying each year with diabetes, one is driven to conclude that the duration of life of a diabetic Indian in Arizona is thirty-five years or that death certificates for Indians are faulty and fail to include the word "diabetes" where it belongs as a primary or secondary cause. Furthermore, the number of Indians with diabetes in Arizona compared with the total number of diabetic patients in the state bears essentially

4. Morrison, H.: Boston M. & S. J. 175:54 (July 13) 1916.

5. Salsbury, C. G.: Disease Incidence Among the Navajos, Southwest. Med. 21: 230-233 (July) 1937.

the same relative proportion, 10 per cent, as do Indians to the total population. Diabetes in Arizona is just as common among Indians as among the rest of the population.

If the survey covered only two thirds of the Indians, the number with the disease would be raised from

TABLE 5.—*Diabetes Found Among Arizona Indians*

Total number of diabetic Indians found.....	73
Males.....	42
Females.....	29
Unspecified.....	2
Classification by tribes:	
Pimas.....	21
Apaches.....	12
Papagos.....	10
Mohaves.....	8
Navajos.....	4
Maricopas.....	3
Yavapai.....	2
Comanche.....	1
Laguna.....	1
Unspecified.....	11*
	73

* Two were added in allocating incomplete case reports.

seventy-three to 109, and the duration of diabetes in an Arizona Indian would jump to fifty-four years, which of course is absurd. A physician long associated with work among the Navajos replied to my question "What percentage of Navajos in Arizona ever see or come under the influence of a doctor?" "From 50 to 60 per cent," and to another question, "For what percentage of deaths do you suppose there is really known an accurate cause?" he answered "In our area my guess would be in about 25 per cent; in the back stretches of the reservation a much smaller percentage." Comparing these statements with the two annual deaths reported for the whole state yearly, the inference is clear that death certificates are lacking in accuracy. In fact, for the state as a whole the number of certificates filed "cause of death unknown" exceeds by several times those returned with the diagnosis of diabetes.

Doubting Thomases may say that the Indians had glycosuria but not diabetes. To this I reply that, of the first twelve blood samples sent to the Phoenix Pathological Laboratory from one of the Indian reservations because of suspected diabetes, eleven of the twelve showed hyperglycemia. Again I wish to give credit to

TABLE 6.—*Distribution by Age and Sex of Arizona Diabetic Indians*

Ages	Males	Females
5-14.....	1	0
15-24.....	1	1
25-34.....	4	7
35-44.....	10	7
45-54.....	14	7
55-64.....	9	6
65-74.....	2	1
75 and over.....	1	0
	42	29

Two were added, allocated from incomplete cases, no sex given.

the liberality of that laboratory in making these and many other tests for me at so minimal a sum, at what I like to call "wholesale rates." It represents another example of the "fecundity of the aggregation."

The distribution of Indians by tribes is shown in table 5 and by age in table 6. I would point out that the Navajos are nomads and the Apaches herdsman, and the Pimas depend on agriculture and I understand harvest their crops on shares, allowing the Papagos to do most of the work.

DIABETES AMONG PHYSICIANS IN ARIZONA AND RHODE ISLAND

If diabetic mortality statistics are even an approximately accurate index of the incidence of diabetes in a community, one would expect this to be reflected in the incidence of diabetes among physicians. Therefore an investigation of diabetes occurring in doctors was made in Arizona and later, to test the validity of the comparison of its low diabetic mortality of 10 per hundred thousand with that of 42 in Rhode Island, or as adjusted for the two states for age and sex, 13 and 37, a similar survey was carried out in exactly the same way and among the same number of doctors in Rhode Island. If diabetes is one fourth or one half as frequent in Arizona as in Rhode Island, the signed testimonies of the physicians in these states do not show it. The results were practically identical. In each state requests were sent to 562 doctors, and to those who did not reply to the first request a subsequent letter was forwarded. Three hundred and thirty-nine doctors reported in Arizona and of these there were eight with diabetes, or a ratio of one diabetic doctor to forty-two nondiabetic doctors. In Rhode Island the responses were somewhat more liberal. In all, 392

TABLE 7.—*Comparison Between Diabetic Physicians in Arizona and Rhode Island*

	Arizona	Rhode Island
Total physicians.....	562	938
Physicians in survey.....	562	562
Total reporting.....	339	302
Diabetic.....	8	11
Average age.....	62.0 years	61.0 years
Nondiabetic.....	323	381
Average age.....	47.3 years	49.1 years
Diabetic to nondiabetic physicians.....	1:42	1:36

physicians have so far reported and eleven stated that they had diabetes, making a ratio of one to thirty-six. The average age of the doctors reporting no diabetes in Arizona was 47 years and in Rhode Island 49 years, whereas the average age of those with diabetes in Arizona was 62 and in Rhode Island 61 years. Diabetes does not spare doctors in Arizona.

An estimate of the morbidity of diabetes among physicians in the United States can be made by a study of the deaths from the disease as reported by the American Medical Association.⁶ These amounted to ninety-one for the year 1939. The total number of doctors in the country at that time was stated to be 169,682. There was, therefore, one death of a doctor with diabetes for each 1,891 physicians. If we assume that the duration of the diabetes among doctors is ten years, then the number of physicians living in the United States with diabetes would be one in 189. If we further assume a duration of twenty years, it would be reduced to one in ninety-four. Therefore, among the 562 doctors in Arizona one would expect three with diabetes on the basis that doctors lived ten years or six with diabetes if they lived twenty years. As a matter of fact, eight doctors were found in Arizona with diabetes, or one diabetic doctor for every forty-two physicians, or fully up to expectations. Of course, I am dealing with small numbers.

6. Obituaries of Physicians Published in 1939, editorial J. A. M. A. 114:1362 (April 6) 1939.

DIABETES AMONG CLERGYMEN IN ARIZONA

Doctors and ministers in Arizona are approximately equal in number. Curiosity led me to attempt a survey of the incidence of diabetes among the clergy. The replies were far less numerous. Thus, of 531 clergymen only eighty-eight responded, and only two of these

TABLE 8.—Present Age of Diabetic Persons in Arizona

	Males					Females					Total Male and Female
	Mexicans	Indians	Whites, Including Jews	Negroes	Others	Mexicans	Indians	Whites, Including Jews	Negroes	Others	
Under 14	0	1	11	0	0	1	0	9	0	0	22
15-24	1	1	23	1	0	3	0	22	0	0	51
25-34	1	4	24	0	1	3	8	17	1	0	59
35-44	4	10	33	1	0	8	6	30	3	0	95
45-54	8	13	52	2	2	22	6	60	2	1	168
55-64	9	8	54	2	3	15	5	64	4	0	164
65-74	2	2	46	1	0	5	1	57	3	0	117
75+	0	1	13	0	0	1	0	9	0	0	24
Totals	25	40	256	7	6	58	26	268	13	1	700*

* Plus fifty-five incomplete cases (thirty-one females and twenty-four males).

stated that they had diabetes, a ratio of one to forty-four. However, other methods of investigation disclosed three more ministers with diabetes, so that finally the ratio of diabetes among ministers replying was one in forty-four, but of all those investigated was five or one for each 106 ministers, if it is assumed that we had reports for each one of the ministers in the state. The ages of the ministers I do not know.

DIABETES AMONG PRISONERS

The investigation of diabetes among the Indians in Arizona was handicapped because of their inaccessibility. The density of population on the Navajo reservation is only about 1.5 Indians to a square mile. Even with an automobile, hunting diabetic Navajo Indians is a rather exhausting sport, and to give myself a brief respite I turned to two areas where the task would be easier and there would be no worry that any person with diabetes would escape the Benedict test. In Florence is an institution admirably adapted for the purpose, and the state prison there furnished me with some 800 subjects. My preliminary inquiry was disappointing, but the superintendent and the prison physician were so cooperative that now I have the privilege of reporting that in the state prison at Florence where one diabetic individual was expected by National Health Survey tabulations, three were found, a higher percentage than on Riker's Island in New York. Just why diabetes appears more frequently among prisoners in Arizona than in New York I cannot say. At any rate I can report that the blood sugar tests of the three diabetic prisoners, as made at the Phoenix Pathological Laboratory, showed 342 mg., 458 mg. and 368 mg. respectively. The ages of the diabetic prisoners ran true to form. The average age for the diabetic prisoners was 46.6 years. Furthermore, obesity ruled among the diabetic in the Arizona State Prison just as it does in Boston. The average weight for all the prisoners was 152 pounds (69 Kg.), but the average weight of the diabetic prisoners was 194 pounds (88 Kg.). If prisoners weigh so much in Arizona, the question arises as to what the weights are for citizens of Arizona. It would be desirable to secure weights of Indians, particularly the Navajos and Pimas.

DIABETES AMONG THE INSANE

The state mental hospital in Phoenix furnished another group where one could be sure that tests for diabetes were performed on all inmates. The search for diabetic patients revealed that among an approximate thousand inmates there were fourteen with diabetes instead of the six expected. For comparison are available figures for the 26,031 mental patients in Massachusetts, among whom 219 were diabetic, or a ratio of 8 per 10,000. In other words, diabetes among the prisoners and insane in Arizona ranks high and apparently fully as high as if not higher than in similar populations in New York and Massachusetts.

TOTAL NUMBER OF DIABETIC PERSONS IN ARIZONA

The survey disclosed 755 diabetic persons in Arizona. The distribution by sex was as expected: males 358 and females 397. The age distribution was the same as that for other areas and is shown in table 8.

The crux of the situation, however, is to determine what percentage of the inhabitants of the state was covered by the survey; that I do not know, but it has been variously estimated from a low of 40 per cent for Mexicans to a high of 75 per cent for the white population. The census of 1940 will be helpful and, in fact, essential in this regard. I do not wish to enter into a detailed discussion of the various methods that could be employed to enable one to compare the morbidity incidence of Arizona for diabetes with that in other sections of the country in order to test the reliability of its mortality statistics. However, I will briefly enumerate some of them.

The number of diabetic persons in Massachusetts has been a subject of close study for many years. It was here that the first field work was done on chronic disease and therefrom certain conclusions could be drawn. Dr. Lombard and I also investigated the death certificates of 744 diabetic patients previously treated by me and found that only 62.9 per cent were so classified on the death records. Even if all had had the word "diabetes" on the death certificate only 82.5 per cent of the total number would have been thus classified by the joint causes of death. Thus the mortality from

TABLE 9.—Diabetic Persons Expected and Found in Arizona

	Cases Expected, Whole State	Cases Expected, Surveyed Population *	Cases Reported in Survey	Per Cent Ratio Cases Reported to Those Expected in Surveyed Population
Total population.....	1,168	537-747	755	101-141
Males.....	529	243-338	358	106-147
Females.....	639	294-409	397	97-135
White.....	797	382-526	545	107-148
Mexican.....	223	89-131	89	66-100
Indian.....	115	57-77	73	95-128

* Based on estimate coverage of population in survey as follows: white: urban 60-75 per cent; rural 40-60 per cent; Mexican: 40-60 per cent; Indian: 50-60% per cent; others (same as white). Mexican population known to have decreased since 1930.

diabetes as recorded in the death records represents about two thirds of the mortality of persons with the disease and four fifths of the true mortality as measured by the joint causes of death.

During the last eleven years, beginning in 1929, in Arizona there have been 438 recorded deaths from diabetes, the low figure occurring in 1934 and the high figure in 1939. That makes an average of forty deaths a year. If it is assumed that this figure, as in Massachusetts, represents only 62.9 per cent of the deaths,

the total number of persons dying in the state with diabetes would have averaged for this period sixty-four annually. If this figure is multiplied by ten as a fair estimate for the duration of diabetes, the expected number of diabetic persons in the state would be 640, but this number is based on the whole state whereas the survey showed 755 deaths for a part of the state.

In determining the extent of the state covered, one might base it on the number of physicians reporting diabetes or no diabetes as compared with the total number of physicians, which this February in Arizona I thought, from all I could learn, to be 562. Furthermore, this proportion would be 290/562 and for the

TABLE 10.—Diabetes Death Rate (Number per Hundred Thousand Estimated Population)

	1938 *	1937	1936	1935	1934	1933
Alabama.....	10.6	12.3	9.1	10.9	9.9	
Arizona.....	10.7	10.0	10.8	9.9	7.6	8.0
Arkansas.....	9.2	8.9	7.9	7.8	8.1	
California.....	25.3	23.7	24.4	21.7	22.9	
Colorado.....	17.9	18.4	16.1	13.8	13.1	
Connecticut.....	30.3	32.5	29.2	30.5	26.6	26.9
Delaware.....	28.4	29.3	30.5	26.9	28.8	
District of Columbia.....	26.6	28.1	26.7	25.9	33.2	27.3
Florida.....	19.7	17.7	18.6	19.5	17.0	15.8
Georgia.....	12.6	12.5	12.9	12.7	11.7	
Idaho.....	14.4	15.4	17.7	19.4	16.7	16.3
Illinois.....	27.6	29.9	26.1	28.4	26.1	
Indiana.....	25.3	24.6	24.7	22.3	23.8	22.0
Iowa.....	22.5	24.5	20.9	24.4	22.8	
Kansas.....	23.9	24.1	24.1	22.5	24.4	23.6
Kentucky.....	13.9	15.1	14.5	15.2	14.0	
Louisiana.....	17.6	17.5	15.8	13.5	13.6	
Maine.....	26.6	23.4	28.1	27.7	28.4	28.7
Maryland.....	28.6	26.3	27.5	27.1	23.8	23.7
Massachusetts.....	33.7	31.4	29.7	30.3	28.2	
Michigan.....	26.2	26.8	26.0	23.7	23.5	
Minnesota.....	26.5	24.5	26.2	22.8	23.3	21.5
Mississippi.....	12.6	12.4	11.9	11.1	11.3	
Missouri.....	20.6	22.6	20.7	23.0	22.4	
Montana.....	21.9	21.9	23.5	21.1	22.4	17.1
Nebraska.....	25.1	26.1	26.2	24.7	26.0	23.8
Nevada.....	16.8	18.8	15.0	13.1	17.3	16.7
New Hampshire.....	33.7	31.4	31.1	29.1	29.4	26.0
New Jersey.....	29.6	30.8	30.5	28.3	27.2	28.7
New Mexico.....	8.1	8.8	8.5	9.2	9.5	
New York.....	36.9	35.8	32.6	32.3	31.8	
North Carolina.....	11.1	11.9	10.7	11.4	11.0	
North Dakota.....	17.1	18.8	18.6	19.7	20.1	
Ohio.....	26.7	27.4	25.9	25.1	23.8	
Oklahoma.....	12.3	14.6	12.3	12.0	10.6	
Oregon.....	25.9	23.3	25.0	20.5	22.4	
Pennsylvania.....	31.3	27.9	27.9	27.4	26.1	
Rhode Island.....	41.9	42.0	33.8	33.0	33.9	35.9
South Carolina.....	11.7	11.8	12.2	11.9	11.2	
South Dakota.....	18.5	19.1	21.7	19.1	23.0	18.9
Tennessee.....	11.4	11.6	11.7	10.9	10.7	
Texas.....	12.6	12.7	11.7	11.8	11.6	
Utah.....	20.8	18.5	20.3	17.9	17.5	13.5
Vermont.....	30.3	24.5	25.5	30.8	37.2	28.6
Virginia.....	17.0	16.5	16.0	17.4	15.0	
Washington.....	24.8	23.5	24.8	23.1	21.4	22.0
West Virginia.....	15.2	14.6	14.2	12.0	12.4	
Wisconsin.....	30.3	26.6	30.0	26.3	25.1	24.2
Wyoming.....	17.4	17.9	15.5	17.2	10.4	13.5

* Rates based on 1937 population; no estimate made for 1938.

whole state the number of persons with diabetes would be raised from 755 in the survey to 1,471. Objections may be made that the physicians not reporting at all may have more or less diabetic patients than those reporting. The answer to that no one can give.

The number of diabetic persons in Massachusetts has been most carefully estimated and if the number 17,500 is divided by the number of physicians practicing in Massachusetts, 7,528, the number of patients reported by each physician. If this same method is applied to the 290 physicians reporting 755 diabetic patients, there are 2.6 per physician in Arizona.

Still another method is available, namely to assign to the state the expected number of diabetic persons based on the National Health Survey and at the same time with arbitrary allowances for coverage for the various types of population. For this special calculation I am indebted to Mr. Marks.

The calculation shows that for all groups save Mexicans, and the indications are that the Mexican population has decreased appreciably since 1930, the percentage ratio cases reported to those expected in the population surveyed met the requirements at both the lowest and the highest estimations of coverage.

Of far greater significance in my own mind than these various estimations are the following two letters of approval which I have received respectively from Dr. Lombard, and Dr. Dublin and Mr. Marks.

At the present time when the available census records are ten years old it is impossible to compute either morbidity or mortality rates with any assurance that they will be reasonably accurate. However, from a careful study of the morbidity data collected by Dr. Joslin and applying to an estimated population of both Arizona and Massachusetts the age specific diabetes morbidity rate obtained in the National Health Survey, an expected number of the cases was such that I am strongly inclined of the opinion that diabetes morbidity does not vary greatly in this country. Mortality does vary and a logical explanation of this would be that for some reason or other many individuals dying with diabetes are not so certified on their death certificates.

HERBERT L. LOMBARD, M.D., Boston.

Low recorded death rates from diabetes, as in Arizona, which you chose for your survey, must not be accepted at their face value. Factors such as age, sex and racial composition of the population, the density of population, economic status, and the number and location of doctors and hospitals all influence the recorded mortality. Thus, it is known that the mere adjustment of death rates to a common sex-age basis reduces appreciably the margin between the diabetes death rates in a state like Arizona and those which have high reported death rates. The rates in Arizona's cities are of the same order of size as those elsewhere in the country. Furthermore, your survey has shown an incidence of diabetes, based on actually reported cases, which after suitable allowance for her low proportion of old people and her high ratio of males to females, very much closer to the average for the country than is found in the mortality data. For the population of the state as a whole, and for the various groups by sex, age and race, the numbers of reported cases approximate, within reasonable limits, the numbers one would expect to find in comparison with the general prevalence of diabetes.

LOUIS I. DUBLIN, Ph.D., and
HERBERT H. MARKS, New York.

June 11, 1940.

CONCLUSIONS

In Arizona the reported diabetic mortality is not consistent with diabetic morbidity. A survey of persons with diabetes in the state conducted by Arizona physicians and myself, granting a reasonable allowance for the number of persons covered in the survey, makes it evident that the incidence of diabetic morbidity in Arizona is comparable to that of the National Health Survey. This held true for all groups including Jews, physicians, ministers, prisoners, the insane, males and females, the white population and the Indian population. Among the Mexican population there was a deficit, as the number of persons with diabetes found was less than the theoretical number expected, for which the explanation may be inaccuracy of population data. Final calculations based on the number of persons with diabetes in Arizona must await the completion of the 1940 census.

A diabetic survey in Arizona supports the thesis that diabetes is universal and conforms to the rule that the incidence of diabetes is highest where (1) the average age is the greatest, (2) women predominate, (3) obesity is most frequent, (4) the proportion of Jews is greatest, (5) medical supervision is closest and (6) deaths are most accurately reported.

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PREDICTION AND PREVENTION OF
PREGNANCY ACCIDENTS IN
DIABETES

PRISCILLA WHITE, M.D.

AND

HAZEL HUNT, A.B.

BOSTON

Our present conception of the mechanism of the accidents in diabetic pregnancies has been the outcome, first, of our realization that adequate dietary control of diabetes and insulin therapy did not lower the fetal mortality rate and, second, our correlation of the behavior of diabetic pregnancies in relation to the balance of pregnancy hormones—chorionic gonadotropin, estrogen and progesterone.¹ We believe (1) that an abnormal rise of chorionic gonadotropin after the twentieth week to a level of 200 rat units per hundred cubic centimeters of blood predicts in the diabetic premature delivery, stillbirth and neonatal deaths, (2) that these accidents are caused by a failure of production or of metabolism of estrogen and progesterone and (3) that they are prevented by continuous substitutional estrogen and progesterone therapy in replacement doses.

These conclusions are based on an analysis of sixty-one completed diabetic pregnancies treated and studied at the George F. Baker Clinic between January 1936 and June 12, 1940. The earlier hormonal analyses were made by Dr. George Van S. Smith and Mrs. Smith in their laboratory to complete their studies in the problem of preeclamptic toxemia of pregnancy, and the later ones have been done in the laboratory of the New England Deaconess Hospital, where we have attempted to establish them on a routine as well as on a research basis.

The sixty-one patients studied fall into three groups, twenty-five whose hormonal balance was normal, twelve whose hormonal balance was abnormal and uncorrected, and twenty-four whose balance was abnormal but who received substitutional estrogen and progesterone therapy.

The clinical course and outcome of the twenty-five normal hormonal diabetic pregnancies was uneventful. None developed preeclamptic toxemia, none had premature deliveries, and fetal survival was 92 per cent. One death was due to asphyxia pallida and one to hemorrhagic disease of the newborn. Contrast this experience with the course of the twelve patients whose values were abnormal and who received no therapy. Nine of the twelve developed preeclamptic toxemia, the remaining three had premature deliveries, and fetal survival was only 42 per cent. From this small group the pattern of behavior of pathologic diabetic pregnancies was clarified to us. Maternal and fetal behavior fell into two groups. After the abnormal rise of chorionic gonadotropin either the mother had a lightning-like toxemia, usually with hydramnios and delivery of a macerated stillborn child, or without toxemia was delivered prematurely of a mature-appearing atelectatic infant dying within a few hours of birth.

From the George F. Baker Clinic of the New England Deaconess Hospital, Elliott P. Joslin, medical director.

Read before the joint meeting of the Section on Obstetrics and Gynecology and the Section on Pediatrics at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. White, Priscilla; Titus, R. S.; Joslin, E. P., and Hunt, Hazel: *Am. J. M. Sc.* 1938: 482 (Oct.) 1939.

Prevention of the accidents was our next problem. At the suggestion of the Smiths,² substitutional estrogen and progesterone therapy in replacement doses was started. Thirteen patients were given daily doses of from 150,000 to 450,000 international units of estradiol and from 10 to 40 mg. of benzoate proluton. Toxemia was controlled, premature deliveries did not occur, and fetal survival was 92 per cent. Though successful, this treatment would have been no more than a physiologic curiosity because of prohibitive cost but was supplied for these investigations through the courtesy of a manufacturer. Our next problem was the substitution of something inexpensive and preferably oral for estradiol benzoate and proluton. Through a grant from the National Research Council this study has been made possible, and eleven patients have been treated with oral stilbestrol in doses of 40 to 120 mg. daily and pregnolin 10 to 40 mg. daily, the stilbestrol being supplied through the courtesy of another manufacturer.

The clinical results are comparable: Toxemias were controlled, no markedly premature deliveries occurred and, barring one case of fatal erythroblastosis, the third erythroblastic infant of this mother, the fetal survival was excellent, 90 per cent. The one failure had perfectly controlled diabetes but imperfectly controlled hormonal balance, developed toxemia and delivered normally a typical gigantic macerated fetus.

Our present plan of treatment is oral therapy, but if the gonad stimulating factor called "prolan" is not falling to satisfactory levels after two weeks' adequate trial with stilbestrol in doses up to 120 mg. daily, stilbestrol given intramuscularly up to 50 mg. is substituted for the oral preparation. Among sixteen patients who have been or are being treated with massive doses of stilbestrol, no side reactions have occurred and no toxicity measured by bilirubin excretion tests has been observed.

Let us compare the fetal survival in our three groups: 92 per cent when the hormonal balance was normal, 42 per cent when the balance was abnormal and uncorrected and 87 per cent, including the case of erythroblastosis, when the abnormal balance was corrected.

The high level of late fetal mortality, namely 33 per cent, which was our yearly rate until 1938, is the one reported among diabetic clinics throughout the world. Obstetric hospitals have reported lower rates, we believe, because of the difference in patient clientele. Obstetric hospitals see many short duration cases with onset of diabetes in pregnancy, transitory hyperglycemia and glycosuria—patients whose clinical course and endocrine balance is different from that of chronically progressive diabetes. Diabetic clinics see more cases of diabetes of long duration with pregnancy incidental to the disease. Since our own practice is consultative, we refer back the borderline and short duration cases and deliberately select potentially abnormal cases. But the value of this presentation lies in this very fact—the obstetrician will see more patients of this type, for not only does one girl in 2,500 contract diabetes, but after many years' duration of the disease she will now live to the child-bearing age.

Delivery depends on clinical and hormonal behavior. Cesarean section is favored in the abnormal group, normal delivery in the normal group.

The treatment of diabetes is the simplest part of our problem. The diet must be adequate, carbohydrate liberal, from 150 to 250 Gm., protein 2 Gm. per

2. Smith, George Van S., and Smith, Olive Watkins: *Am. J. Obst. & Gynec.* 39: 405 (March) 1940.

kilogram of body weight, fat to complete the caloric prescription of 30 calories per kilogram. Medicinal minerals and vitamins are added. Insulin dosage, to avoid the pitfalls of low renal threshold, is controlled by blood rather than urinary sugars.

In a group of sixty-one patients we believe we have demonstrated that the accidents commonly seen in diabetic pregnancies are not due to imperfectly controlled diabetes but to an abnormal hormonal balance, a rise of chorionic gonadotropin, fall of estrogen and progesterone. These accidents are prevented by continuous substitutional estrogen and progesterone therapy in replacement doses. Finally, we believe that this treatment is no longer a physiologic curiosity but one well within the field of practical therapeutics.

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THE NEONATAL PROBLEM IN INFANTS OF DIABETIC MOTHERS

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Infants of mothers with diabetes mellitus show a high morbidity and mortality rate. My object in this paper is to present sixty-five consecutive infants of diabetic mothers studied during the past ten years. Such a group of infants was almost nonexistent two decades ago, before the insulin era. Women with diabetes either did not become pregnant or failed to give birth to a living child. Since the insulin era, the fecundity of the diabetic woman has greatly increased, and the juvenile diabetic patient has now reached the childbearing age. There is, therefore, an increasing number of pregnant women with diabetes mellitus and an increasing number of infants of diabetic mothers.

This group of infants has not been studied in large enough numbers to permit definite conclusions. There are sufficient data, however, to warrant certain general conceptions with regard to these infants. Miscarriages and stillbirths are most common in this group.¹ There has been a great variation in the mortality rate, and reports showing rates as high as 40 per cent have been recorded. A second conception is that these babies are unusually large and are frequently called "giant infants" at birth.² There is no evidence, however, to show that the skeletons of these infants are larger than normal or that these babies develop into larger types. A third conception from previous studies is that these infants are frequently born with hypertrophy of the islands of Langerhans. Recent work³ has shown that the majority of the infants studied have this condition, although it may also be found in normal infants. A further prevalent conception is that these infants frequently present symptoms due to hypoglycemia.⁴ For this reason it has been advocated that all infants of diabetic mothers be given parenteral dextrose immediately after birth. Recent observations,⁵ however, have not confirmed this idea.

Read before the joint meeting of the Section on Obstetrics and Gynecology and the Section on Pediatrics at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Joslin, E. P.: *The Treatment of Diabetes Mellitus*, Philadelphia, Lea & Febiger, 1940, p. 693.

2. Fischer, L.: *Zentralbl. f. Gynäk.* 59:249 (Feb. 2) 1935.

3. Helwig, E. B.: *Hypertrophy and Hyperplasia of Islands of Langerhans in Infants Born of Diabetic Mothers*, *Arch. Int. Med.* 65:221-239 (Feb.) 1940.

4. Randall, L. M., and Rynearson, E. H.: *Delivery and Care of the Newborn Infant of the Diabetic Mother*, *J. A. M. A.* 107:919 (Sept. 19) 1936.

5. Miller, H. C., and Ross, R. A.: *Relation of Hypoglycemia to the Symptoms Observed in Infants of Diabetic Mothers*, *J. Pediat.* 16:473 (April) 1940.

The material for the present study has been afforded by the clinic of Dr. Elliott P. Joslin of Boston. I myself have observed these sixty-five infants throughout the neonatal period. The care of the mothers has been uniform and has been modified only by newer concepts of diabetic treatment. One obstetrician has delivered all these babies.⁶ Analgesics prior to delivery were given to some of the mothers in this series. Most of the babies have been delivered by cesarean section under spinal anesthesia without preoperative medication. There have been no maternal fatalities.

The procedure adopted for the care of these babies has been as follows: The infant is immediately drained and all material obstructing the upper respiratory passages is removed by suction. If the infant is sluggish in breathing, no mechanical effort is made to resuscitate it. The baby is placed in an incubator with controlled conditions of heat, humidity and oxygen and left in this atmosphere for at least twenty-four hours. Nothing is given by mouth during this period. If the infant's condition is satisfactory, small doses of dextrose are started on the second day. From 1 to 2 drachms (4 to 8 cc.) of 5 per cent dextrose is given at first, and this amount is increased by from 1 to 2 drachms each feeding until 1 ounce (30 cc.) is given. All precautions are taken to avoid infection. Attempts have been made to have these infants nurse, but in general this has been unsuccessful. Microdeterminations of the blood sugar are made on the baby directly after birth and every four to eight hours during the first day. If symptoms do occur the oxygen atmosphere is continued and emphasis is placed on the importance of removal of material from the upper respiratory tract. It was a routine procedure during early observations to give parenteral dextrose directly after birth regardless of the blood sugar determinations. This procedure has not been carried out recently. A careful physical examination has been made on each infant during the first day of life. Tests for syphilis have not been made on these babies but tests on the mothers have given negative results in all cases.

This series of sixty-five infants of diabetic mothers has been divided for the purpose of study into three groups. The first group consists of thirty-seven infants, or 57 per cent of the total, who were normal at birth and whose course during the neonatal period was uneventful. There have been included in this group a few babies who were somewhat sluggish in breathing and who had minor degrees of cyanosis but who were not considered distinctly different from a great many so-called normal babies directly after delivery. Table 1 shows that 35 per cent of these infants were born of mothers who had had diabetes for from ten to twenty years and that 78 per cent of the infants were delivered by cesarean section. In this group 86 per cent were delivered between the eighth and the ninth month of gestation. The babies varied greatly in weight but the majority weighed between 6 and 10 pounds (2,720 and 4,535 Gm.). There were many mothers in this group who showed symptoms of preeclamptic toxemia.

The second group of this series consists of sixteen infants who survived but presented definite major symptoms, which generally occurred directly after delivery. These symptoms were not uniform. The infant would generally cry well at birth and be slightly sluggish in attaining normal color but at the end of two or three hours would develop a slight respiratory grunt. This

6. The mothers of the infants in this series were under the obstetric care of Dr. R. S. Titus and under the medical care of Dr. Priscilla White.

gradually became more accentuated, and the respirations often reached from 100 to 110 a minute. The reflexes usually became distinctly suppressed and crying could be elicited with difficulty. Jerky movements of the extremities were not infrequent and there invariably developed varying degrees of cyanosis. These symptoms usually persisted during the first twenty-four hours and rarely lasted more than two days. The baby's condition was generally improved by oxygen. Parenteral dextrose was given to a number of these infants without change in symptoms.

TABLE 1.—*Summary of Thirty-Seven Infants, Born of Diabetic Mothers, Who Presented No Major Symptoms*

	Duration of Diabetes		Delivery, Cesa-rean	Month of Gestation			Infants' Weight, Pounds	
	1-10 Yrs.	10-20 Yrs.		7	8	9	4-6	6-10
Number	24	13	29	5	16	16	5	32
Per cent	65	35	78	14	43	43	14	86

Physical examination of these infants directly after birth showed no demonstrable cardiac abnormality. The respiratory murmur over the lungs was frequently suppressed and was considered to indicate a marked degree of primary atelectasis. Some of the infants showed definite edema of the extremities and face.

In this group of sixteen infants, 31 per cent of the mothers had had diabetes for a period of from ten to twenty years (table 2). About a third of the mothers showed definite signs of preeclamptic toxemia with elevation of blood pressure, edema and albuminuria. Fifty per cent of these infants were delivered by cesarean section and all were born between the eighth and the ninth month of gestation. The weights of these babies were not unusual.

The following histories are examples of infants in this group who presented major symptoms:

REPORT OF CASES

CASE 29.—A female infant was delivered by cesarean section of a woman aged 24, who had had recognized diabetes for four years. The mother had been receiving approximately 14 units of regular insulin and 34 units of protamine zinc insulin late in her pregnancy. Her diabetes and pregnancy were uncomplicated. Her catamenia had been regular. This was her first pregnancy.

Cesarean section was done because the fetus was considered exceptionally large for the estimated eighth month of gestation. The baby at birth presented the appearance of a full term, mature infant. She weighed 8 pounds 10 ounces (3,912 Gm.). The dimensions were as follows: length 51 cm., head circumference 34 cm., thorax 33 cm. The delivery was performed under spinal anesthesia without preoperative medication. The placental attachment was beneath the uterine incision. The infant was not considered unusually cyanotic at birth and cried satisfactorily. There developed soon after birth a respiratory grunt, and considerable cyanosis of the extremities persisted. Thin yellowish fluid resembling amniotic sac contents was aspirated repeatedly from the trachea and recovered by postural drainage. There developed during the first few hours extreme degrees of general cyanosis with very shallow respiratory excursions. These attacks were apparently relieved by oxygen. The baby received 65 cc. of 5 per cent dextrose by hypodermoclysis six hours after birth. After twelve hours, because of persistent cyanosis, the baby was placed in a respiratory chamber in an atmosphere of helium and oxygen. The baby had no further marked cyanotic attacks but otherwise showed no improvement. At the end of the second day there were general hypotonicity, cyanosis of the extremities, no nursing reflex and a persistent respiratory grunt. Without any change in treatment, respirations gradually decreased from 120 a minute to normal, the

extremities became persistently pink and the baby cried vigorously. When about 60 hours old, the baby was taken out of the oxygen chamber and appeared essentially normal. No physical abnormalities were noted at this time and the infant's convalescence was uneventful. The baby lost 1 pound (450 Gm.) during the first four days. A solution of 5 per cent dextrose in teaspoon amounts was started after the infant was taken from the oxygen chamber.

The baby's blood sugar was 180 mg. per hundred cubic centimeters at birth, 170 mg. at 8½ hours, 160 mg. at 24 hours, 60 mg. at 32 hours and 60 mg. at 36 hours.

CASE 49.—A male infant was the first child of a mother, aged 25, who had had diabetes for fifteen years. Her disease was severe but well controlled. Her catamenia had been irregular but at the time of delivery physical examination suggested an eight months gestation. The pregnancy was uncomplicated except for a severe secondary anemia.

The baby was delivered by cesarean section under spinal anesthesia. Pentobarbital sodium 4½ grains (0.3 Gm.) was given preoperatively. The infant's birth weight was 6 pounds 6 ounces (2,892 Gm.). He reacted normally after birth. The cord blood sugar was 60 mg. per hundred cubic centimeters. Four hours after birth he became very cyanotic. Eight hours later the condition became worse, respirations were very shallow and convulsive movements of the extremities developed. The baby was considered moribund. At this time the blood sugar was 9 mg. per hundred cubic centimeters. Thirty cc. of 10 per cent dextrose solution was given by gavage and clinically there was great improvement in the patient's condition. The blood sugar rose to 30 mg. on the second day and to 80 mg. on the third day. He lost 10 ounces (283 Gm.) but showed no further symptoms. His reactions suggested an immature infant. Physical examination was negative and the future course was normal.

The mother was given insulin preoperatively and showed symptoms of insulin shock after delivery. Her blood sugar at that time was 50 mg. per hundred cubic centimeters.

CASE 1.—A male infant was born of a mother, aged 27, who had had diabetes for twenty years. She was a very small person, weighing about 100 pounds (45 Kg.), but members of her family were large and her husband was of average size. The mother's catamenia had been regular and this was her first pregnancy. She had many complications of diabetes and evidence of toxemia, with elevation of blood pressure and edema of the extremities. The latter disappeared with rest in bed and treatment with stilbestrol and pregnolinine. The baby was delivered under spinal anesthesia without preoperative medi-

TABLE 2.—*Summary of Sixteen Infants, Born of Diabetic Mothers, Who Presented Major Symptoms*

	Duration of Diabetes		Delivery		Month of Gestation		Infants' Weight, Pounds	
	1-10 Yrs.	10-20 Yrs.	Cesa-rean	Unclas-sified	8	9	6-7	7-12
Number	11	5	8	8	10	6	4	12
Per cent	69	31	50	50	63	37	25	75

cation by cesarean section about three weeks before term. The mother's dosage of insulin at this time was 22 units of regular and 32 units of protamine zinc insulin daily. There was definite hydramnios.

The infant weighed 9 pounds 14 ounces (4,480 Gm.) and cried lustily at birth. He passed meconium before complete extraction from the uterus. Considerable fluid was drained and greenish material aspirated by catheter. He remained moderately cyanotic for six hours. He had definite apnea and his respirations were irregular, shallow and rapid, increasing to 120 a minute. He was kept in an incubator in an oxygen atmosphere of from 40 to 60 per cent. He had no convulsions. At about 36 hours he was normal and his course was uneventful. He lost 11 ounces (312 Gm.). Physical examination showed no abnormalities. His head was 35 cm. in circumference, thorax 35.6 cm. and length 52 cm.

An x-ray film was taken after twenty-four hours which showed shadows typical of multiple atelectatic areas, suggestive

of inhalation of amniotic sac contents. The blood sugar at 2 hours was 100 mg. per hundred cubic centimeters, at 5 hours 120 mg., at 9 hours 140 mg., at 14 hours 140 mg. and at 23 hours 120 mg. Dextrose solution was started by mouth at 25 hours of age.

The third group of this series of infants of diabetic mothers consists of twelve infants who died during the first three days of life (table 3). The symptoms that these infants presented showed great variation, and there was no common cause for death. The first three infants of this group died of recognized conditions. In cases 32 and 38 the fetuses were nonviable, delivered spontaneously in the fourth or fifth month of gestation. The remaining seven infants of this group were delivered from one to two months prematurely. The weights of these infants, with two exceptions, were from 6 to 8 pounds (2,720 to 3,630 Gm.). These seven infants presented symptoms of anoxia and died within one to fifteen hours after birth. The symptoms of this group of infants were often similar to those observed in the second group except that they were associated with greater degrees of cyanosis and asphyxia. Dyspnea did not seem such a prominent symptom as in the previous group.

occurred. Apnea developed and this was relieved by artificial respiration and suction. Considerable fluid, suggesting amniotic sac contents, was recovered from the pharynx. She was given 50 cc. of 5 per cent dextrose by hypodermoclysis twelve hours after birth. The baby had a severe cyanotic attack three hours later and efforts to establish respiration were unsuccessful.

The cord blood sugar was 117 mg. per hundred cubic centimeters. At 4 hours the blood sugar was 90 mg. and at 12 hours 60 mg. per hundred cubic centimeters.

The clinical diagnosis was prematurity and asphyxia neonatorum. An autopsy was performed which showed primary atelectasis of the lungs, marked hemopoiesis of the liver and some hemorrhage of both adrenals. The pancreas appeared normal. No definite cause of death was determined.

The second baby, a boy, was regarded as normal at birth and weighed 6 pounds 1 ounce (2,750 Gm.). He presented no problems of resuscitation. Physical examination shortly after birth showed that he was a well developed infant with dimensions of the head and thorax somewhat below the average. There was no demonstrable pathologic condition of the heart and abdominal organs. The respiratory note was distinctly suppressed, especially over the upper lobes of the lungs and the left lower lobe. No rales were heard. The respirations were shallow and there was some thoracic retraction. General cyanosis was noted about two hours after birth, which increased but was modified somewhat by high concentrations of oxygen. Mild convulsive movements of the arms and muscles of the

TABLE 3.—Twelve Deaths of Infants of Diabetic Mothers

Case	Mothers				Weight		Duration of Life	Infants	
	Duration of Diabetes	Medication	Delivery	Gestation	Pounds	Ounces		Clinical Diagnosis	Anatomic Diagnosis
4	8 yrs.	Yes	Normal	9 mos.	6	3	40 hrs.	Erythroblastosis	Erythroblastosis
5	3 yrs.	Yes	Normal	9 mos.	7	3	72 hrs.	Hemorrhage of adrenals	No autopsy
53	1 yr.	No	Breech	9 mos.	6	12	20 hrs.	Cerebral hemorrhage	Tentorial tear, cerebral hemorrhage
32	4 yrs.	No	Normal	5 mos.	3	12	45 min.	Prematurity, asphyxia	Cause of death?
38	4 yrs.	No	Normal	5 mos.	3	..	1 hr.	Prematurity, asphyxia	No autopsy
39	3 yrs.	Yes	Breech	7 mos.	4	4	8 hrs.	Prematurity, asphyxia	Prematurity
36	14 yrs.	Yes	Cesarean	7 mos.	6	12	1½ hrs.	Prematurity, asphyxia	Primary atelectasis, partial
40	4 yrs.	Yes	Cesarean	8 mos.	8	1	2½ hrs.	Asphyxia	Prematurity, cause of death?
42	8½ yrs.	Yes	Cesarean	7½ mos.	6	4	10 hrs.	Prematurity, asphyxia	Aspiration of amniotic fluid
41	1 yr.	No	Low forceps	7 mos.	7	..	14 hrs.	Atelectasis, intracranial hemorrhage?, asphyxia	Primary atelectasis
37	11 yrs.	Yes	Breech	7 mos.	4	8	15 hrs.	Prematurity, asphyxia	Primary atelectasis
17	12 yrs.	No	Cesarean	8 mos.	6	1	10½ hrs.	Asphyxia	Cause of death?

Autopsies were performed in ten of the fatal cases and the exact cause of death was determined in two. Primary atelectasis was frequently noted. Evidence of aspiration of amniotic sac contents, hemorrhage of various organs and areas of hemopoiesis was common. Marked hyperplasia of the islands of Langerhans was noted in only one case.

The following histories are examples of infants who died:

CASES 37 and 17.—These two infants were born of the same mother in successive years and were the only pregnancies. The mother was 23 years old at the time of the first pregnancy and had had diabetes for eleven years. She was receiving 28 units of protamine zinc and 16 units of regular insulin during the second pregnancy. Her catamenia had been regular. Her first pregnancy was not associated with the usual signs of toxemia but before the birth of the second baby she had slight edema. The first baby was delivered by breech extraction under nitrous oxide and oxygen anesthesia two months before term. The mother received pentobarbital sodium 4½ grains (0.3 Gm.) and scopolamine ½150 grain (0.0004 Gm.) about four hours before delivery. The second baby was delivered under spinal anesthesia without preoperative medication shortly after the eighth month of gestation.

The first baby, a girl, weighed 4 pounds 8 ounces (2,040 Gm.) and was cyanotic and atonic at birth, with suppression of all reflexes. The general appearance was that of a small, immature infant. She was placed in an incubator with a mixture of helium and 45 per cent oxygen, which relieved the cyanosis temporarily. During the next five hours severe attacks of cyanosis

face developed. About four hours after birth he was given 75 cc. of 5 per cent dextrose by hypodermoclysis and 25 cc. two hours later, without a change in his condition. The cyanosis became more extreme, periods of apnea developed with increased suppression of all reflexes and the infant died about ten and one-half hours after birth.

The blood sugar determinations were 170 mg. per hundred cubic centimeters at birth, 40 mg. at 3 hours and 140 mg. at 9 hours.

The clinical diagnosis was asphyxia neonatorum. An autopsy revealed no evidence of cerebral abnormality. "The lungs were unexpanded and rubbery, noncrepitant and red throughout. Microscopically, only few alveoli were expanded. The pancreas showed moderate hypertrophy and hyperplasia of the islands of Langerhans with increase of the size of the islands and cells. The immediate cause of death was undetermined." The blood sugar level of the heart was 22 mg. per hundred cubic centimeters and of the liver 27 mg.

COMMENTS

Blood sugar determinations by the Folin-Malmros micromethod, as described by McKittrick,⁷ were made on a large number of infants in this series. The purpose of these studies was to determine, if possible, any relationship between existing symptoms of infants of diabetic mothers and the blood sugar levels. Although determinations were made during the first three days in a large number of cases, only the results of the determinations during the first twelve hours are noted, as

7. McKittrick, J. B.: Serial Blood Sugar Determinations in Normal Newborn Infants, *J. Pediat.* 16: 151 (Feb.) 1940.

invariably symptoms noted in this series of infants occurred during this period (table 4 and chart 1). It will be seen that the maximum blood sugar levels during the first twelve hours were unusually high, namely from 170 to 260 mg. per hundred cubic centimeters, and that

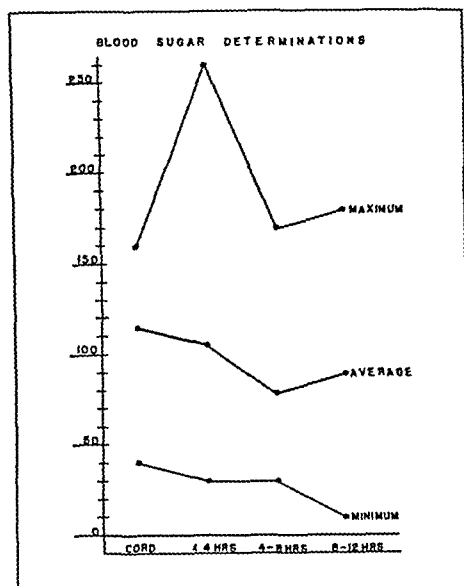


Chart 1.—Curves of maximum, average and minimum blood sugar values, based on determinations made on fifty infants born of diabetic mothers.

the average blood sugar levels during this period were much above the level usually described as normal for an infant of this age. The minimum levels were somewhat lower than the expected but, with one exception, were not unusual, especially if one compares the values given for normal immature infants during the first forty-eight hours of life, as noted by Miller and Ross.⁵ The finding of 9 mg. per hundred cubic centimeters was noted in one infant (case 49), whose mother had had a large dose of insulin shortly before delivery and developed an insulin reaction after the birth of the baby. This infant's condition was greatly improved after the administration of dextrose. It is obvious from these studies that the infants in this series presenting major symptoms during the first twelve hours may have normal

or more, and seven babies who weighed 9 pounds (4,080 Gm.) or more. Studies of these babies through the neonatal period and infancy have offered no evidence that skeletally these infants were larger than normal. There have been many instances in which infants have been delivered from one to two months prematurely and have weighed 8 pounds or more.

This study of sixty-five consecutive infants of mothers with diabetes mellitus emphasizes again the high morbidity and mortality rates in the neonatal period. In this series 43 per cent of the infants, as shown in table 5, showed clinical symptoms, and 18 per cent of the sixty-

TABLE 5.—Outcome of Sixty-Five Infants Born of Diabetic Mothers

Group	No. of Cases	Per Cent	Result
1	37	57	Normal course
2	16	25	Abnormal symptoms
3	12	18	Fatalities

five died. In two of the fatalities the fetuses were undoubtedly nonviable, a third had erythroblastosis, a fourth had cerebral hemorrhage with a tentorial tear and a fifth probably had hemorrhagic disease of the newborn. If these five fatalities are excluded, a corrected mortality rate would be 11 per cent. The symptoms that these infants presented cannot be regarded as specific of the infant of the diabetic mother, but there seems to be a rather typical symptom complex. It usually occurs in the first twelve hours of life and is associated with frequent and labored respirations. A moderate degree of cyanosis also is seen, but this is not extreme except in the terminal stages. Physical examination in general shows evidences of unexpanded lungs and occasional edema of the subcutaneous tissue. All reflexes are suppressed, but muscular contractions of the face and extremities are not uncommon. The cause of these symptoms cannot be explained by the use of analgesics and anesthetics, since most of the infants were delivered under spinal anesthesia without preoperative medication. The condition suggests an

TABLE 4.—Blood Sugar Determinations—Males and Females

	Cord	Birth to 4 Hours	4-8 Hours	8-12 Hours
Maximum.....	160	260	170	180
Average.....	113.4	104.5	79.2	89.2
N.....	40	30	30	9
	23	38	34	28
	23	31	27	25

blood sugar levels, as seen in chart 2. Furthermore, it was a common experience that parenteral administration of dextrose failed to relieve the symptoms, as illustrated in chart 2 (case 17).

It has been impossible to add accurate data in this series with regard to the possible effect of maternal diabetes on the weight of the infant. The problem is complicated by the fact that many women with diabetes have an irregular catamenia and also by the fact that 63 per cent of the infants studied were delivered by cesarean section before term. It is the distinct impression from observations at hand that the infants in this series weighed more than the average and that this is due to an excess of adipose tissue. There were fourteen babies in this series who weighed 8 pounds (3,630 Gm.)

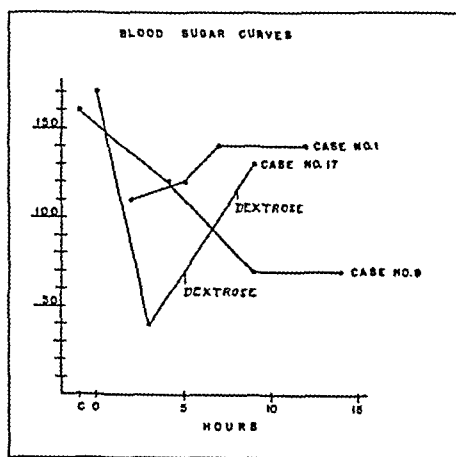


Chart 2.—Curves of blood sugar values of three infants born of diabetic mothers.

intra-uterine cause with involvement of the respiratory center. In many instances a precipitating cause has seemed to be the insufflation of amniotic sac contents.

The symptoms appear to have little relationship to the severity or duration of the mother's diabetes, as seen in table 6. Delivery by cesarean section did not appear to have an unfavorable effect on the infant, as

78 per cent showing a normal course were delivered by this method. Symptoms occurred almost twice as frequently if the infant was delivered in the eighth month of gestation, and 58 per cent of the fatal cases occurred when the infant was delivered in the seventh month. Although this study may clearly suggest the unfavorable influence of interrupting gestation before the eighth month, it should be remembered that the incidence of miscarriages and macerated fetuses among infants of diabetic mothers is not uncommon, and therefore prolonging gestation may be a greater hazard than inducing premature birth.

The study on the blood sugar levels of these infants has been disappointing as far as showing any relationship between the presenting symptoms and hypoglycemia. Experience showed early in the study the importance of maintaining a high maternal blood sugar level before delivery of the infant. It is probable that this fact modified our procedure with regard to the routine administration of parenteral dextrose to the infant of the diabetic mother directly after delivery.

TABLE 6.—*Relation of Diabetes, Type of Delivery and Period of Gestation to Viability of Fetus*

	Num- ber of Cases	Duration of Diabetes		Delivery		Month of Gestation			Infants' Weight Under 5 Pounds
		1-10 Years	10-20 Years	Cesa- rean	Unclas- sified	7	8	9	
Normals	37	65%	35%	78%	22%	14%	43%	43%	8%
Symptoms	16	69%	31%	50%	50%	63%	37%		
Fatalities	12	75%	25%	33%	67%	58%	17%	25%	33%

CONCLUSIONS

1. In a consecutive series of sixty-five infants born of diabetic mothers, 57 per cent were normal and 43 per cent presented symptoms in the neonatal period. The mortality rate was 18 per cent.

2. The symptoms presented by these infants varied greatly and were caused by many conditions. Cerebral anoxia with involvement of the respiratory center appears to be the cause of many of the symptoms presented by these infants.

3. All infants of diabetic mothers should be adequately drained and placed in an atmosphere of from 40 to 50 per cent oxygen immediately after birth.

4. Infants of diabetic mothers in this series showed high blood sugar levels. Hypoglycemia is a rare complication but may occur if insulin is given the mother shortly before delivery. The routine administration of parenteral dextrose immediately after birth is not indicated.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. WHITE AND HUNT AND DR. SISSON

DR. J. A. LAMPHIER, Brooklyn: At the Long Island College Hospital we have observed with considerable interest Dr. White's work regarding the relationship of toxemia in diabetic pregnancies. However, the tremendous dosages and the cost of the drugs have made it beyond our employment for practical application at our clinic. The substitution of stilbestrol for estrogen solves this problem and has answered the question I had in mind. I did not get the name of the substitution therapy for progesterone. I should like to know what drug Dr. White substitutes for progesterone, also the average dose and the average cost of this preparation.

DR. PRISCILLA WHITE, Boston: We have been substituting pregnenolone for progesterone, and we are using less than 50 cents' worth a day. Usually we use only 10 mg. In a few cases we have had to use more than that.

TESTS OF PANCREATIC FUNCTION

MANDRED W. COMFORT, M.D.

ROCHESTER, MINN.

The pancreas is composed of acini lined with columnar cells; between the acini are small groups of cells termed interalveolar cell islets (islands of Langerhans). There are two main types of cells in the islands of Langerhans, distinguished as alpha and beta cells according to special staining reactions of the granules which they contain. The functions of the acinar cells and of the beta cells of the islands of Langerhans are comparatively well defined and progress is being made in the study of the functions of the alpha cells. Tests whereby the functions of each type of cell may be studied will be reviewed, and the clinical use of such tests will be described.

TESTS FOR DISTURBANCES OF EXTERNAL SECRETION OF ACINAR CELLS

The external secretion of the acinar cells is carried by the pancreatic duct to the duodenum. This secretion is under the control of both nervous (vagal) and chemical (secretin) mechanisms. Stimulation of the vagus mechanism produces a juice rich in enzymes, while stimulation of the secretin mechanism produces a juice rich in carbonate. The external secretion of the pancreas thus serves two distinct functions: it acts as a diluting and neutralizing fluid and it provides enzymes important in digestion.

Analysis of Duodenal Content.—Among the earlier tests may be mentioned those in which the gastric content was examined after the administration of test breakfasts and those in which the urine was examined for substances liberated by digestion of capsules swallowed by the patient. These methods have only a historical interest now. Worth while clinical study of secretion of enzymes by the pancreas may be said to have begun with the description of the duodenal tube by Einhorn in 1908. Then, following the establishment of physicochemical conditions governing the activity of enzymes by Sorensen in 1909, adequate methods of chemical analysis were devised, among others by McClure and his associates¹ and by Willstätter and his associates. Many excellent data have been obtained by use of the single barrel tube similar to that described by Einhorn to remove for analysis the fasting content of the duodenum or the content of the duodenum after stimulation with various inorganic substances as well as food. However, a more accurate technic of removing the duodenal content as well as more powerful stimulants now available are requiring restudy of analysis of the duodenal content as a test of external pancreatic function.

Ågren and Lagerlöf² combined previously described methods³ and used a two barrel tube; one barrel entered the stomach and the other entered the duodenum, to

From the Division of Medicine, the Mayo Clinic. Owing to lack of space this article is abbreviated in THE JOURNAL. The complete article appears in the author's reprints.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. McClure, C. W.; Wetmore, A. S., and Reynolds, Lawrence: Physiological Characters and Enzymic Activities of Duodenal Contents During Gastric Digestion in Normal Young Men, J. A. M. A. 77:1468-1469 (Nov. 5) 1921.

2. Ågren, Gunnar, and Lagerlöf, Henrik: The Pancreatic Secretion in Man After Intravenous Administration of Secretin, Acta med. Scand. 90:1-29, 1936.

3. Lim, R. K. S.; Matheson, A. R., and Schlapp, W.: An Improved Method for Investigating the Secretory Function of the Stomach and Duodenum in the Human Subject, Quart. J. Exper. Physiol. 13:353-345, 1922-1923.

remove continuously and separately the gastric and duodenal contents under negative pressure. This technic has eliminated two variables acting on the external pancreatic secretion: first, the intermittent and uncontrolled stimulation of the secretin mechanisms by the entrance of acid gastric content into the duodenum and, second, the diluting effect of the gastric content. It has permitted the quantitative removal of the duodenal content, fractionation of the content as desired and, finally, calculation of the total enzyme activity per unit of time as well as the concentration for each sample. These accomplishments were impossible when the single tube was used. Moreover, the administration parenterally of potent stimulants has insured responses approaching a maximum. Two types of stimulants have been used, one purified secretin and the other those drugs which stimulate the vagus mechanism; each gives characteristic types of secretion and makes possible the selective study of the two functions of external secretion of the pancreas.

Technic of Removal of Duodenal Content with the Double Barrel Gastroduodenal Tube: After a fast of twelve hours a two barrel gastroduodenal tube is introduced into the duodenum. The structure of the tube is diagrammatically shown in figure 1. It is to be noticed that a length of tubing without perforations lies between the perforations in the stomach and those in the duodenum. When the tube is in the correct position that particular portion of the tube not perforated occupies the pyloric portion of the stomach and duodenum. That the tube occupies the correct position is determined by roentgenologic examination of the abdomen. A negative pressure of from 25 to 40 mm. of mercury has been found to be sufficient to prevent to a great extent overflow of gastric juice into the duodenum and for the collection of the duodenal content.

A half reclining position for the patient has been found satisfactory. At the clinic it has been our practice to fractionate the duodenal content into four periods of ten minutes each before stimulation and into four periods of ten minutes each and two periods of twenty minutes each after stimulation.

Secretin as a Stimulant: Physiologists, no doubt, have looked forward to the development of a test of pancreatic function using secretin as a stimulant, since its discovery by Bayliss and Starling in 1902. Although secretin was administered intravenously to a few patients as early as 1926,⁴ it was not until 1934⁵ and 1936⁶ that extensive studies of external pancreatic function were carried out. In most of these studies the single barrel duodenal tube was used to remove the duodenal content. Ågren and Lagerlöf, however, employed the double barrel duodenal tube and reported more results in 1936 that seemed to picture more accurately the type of secretory response to secretin. Their results have been confirmed by Diamond and his associates⁷ and by Osterberg and me.⁸

The effect of secretin administered intravenously is noticeable within a short period of time, usually in a minute. Normal biliary color of the duodenal content rapidly becomes less marked and in many instances a clear, almost colorless secretion is obtained, provided the gallbladder is functioning. The yellowish color of the duodenal content reappears after a short time. In normal persons following stimulation with secretin the volume of duodenal content increased markedly and rapidly, usually reaching its peak within the first ten minute period. The hydrogen ion concentration usually increased one unit and reached a value of 8 or more. The carbonate content increased, roughly paralleling the behavior of the volume. The concentration of enzymes in the juice declined, reaching its low point in the second ten minute period. The total value for each enzyme per unit of time was increased but the increase was almost entirely limited to the first ten minute period,

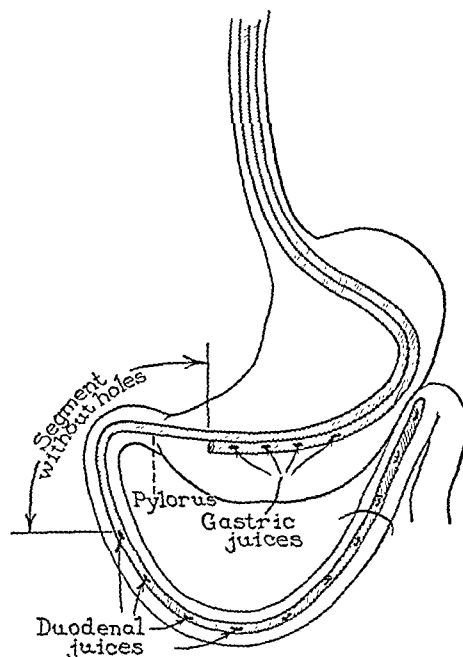


Fig. 1.—Double barrel gastroduodenal tube; one barrel ends in the stomach, the other in the duodenum.

particularly in the case of amylase and trypsin. The increase in total values appears to be due to a washing out of preformed enzymes and not due to any effect of secretin on the formation of enzymes.

The volume, alkalinity, concentration and total excretion of enzymes may be used to detect pancreatic dysfunction, as illustrated in the following case of chronic pancreatitis:

A youth aged 18 years, who registered at the clinic Dec. 12, 1938, had noted a beginning of chronic epigastric soreness, fulness after eating and two or three soft or watery stools daily in June 1937. In December 1937 a severe attack of midepigastric pain extending to the dorsal region required the administration of morphine for relief. Five additional severe attacks had occurred since that time, the last one in September 1938, but three or four mild attacks had occurred weekly. On physical examination slight tenderness in the epigastrium was the only abnormality found. Urinalysis did not disclose glycosuria and the concentration of sugar in the blood was within normal limits but the test for tolerance for dextrose showed a diabetic curve. Hemoglobinemia was present. Leukocytes numbered 15,600 per cubic millimeter, and 81 per cent were neutrophils. The lipolytic activity in terms of twentieth-normal

4. Chiray, Salmon, A. R., and Mercier, A.: Action de la sécrétine purifiée sur la sécrétion externe du pancréas de l'homme (note préliminaire), *Bull. et mémoires Soc. méd. d. hôp. de Paris* 50:1417-1426 (July 30) 1926.

5. Vogtlin, W. L.; Greengard, H., and Ivy, A. C.: The Response of the Canine and Human Pancreas to Secretin, *Am. J. Physiol.* 110:198-224 (Nov.) 1934.

6. Chiray, M., and Bolger, M.: Mesures de la sécrétion pancréatique externe en chienne par l'épreuve à la sécrétine purifiée, *Nutrition* 6:223-230, 1936.

7. Diamond, J. S.; Siegel, S. A.; Gall, M. B., and Karlen, S.: The Use of Secretin as a Clinical Test of Pancreatic Function, *Am. J. Digest. Dis. & Nutrition* 6:366-372 (Aug.) 1939.

8. Comfort, M. W., and Osterberg, A. E.: A Comparative Study of Pancreatic Secretion in Man Following Stimulation with Secretin and Mecholyl Chloride, *Arch. Int. Med.* 66:688-706 (Sept.) 1940.

sodium hydroxide per cubic centimeter of serum was 2.5 cc. and the amylolytic activity in terms of units was 530. A diagnosis of chronic pancreatitis was made and confirmed at exploration in May 1939.

A test of function of external pancreatic secretion using purified secretin intravenously as a stimulant was performed. Figures 2, 3 and 4, in which the values

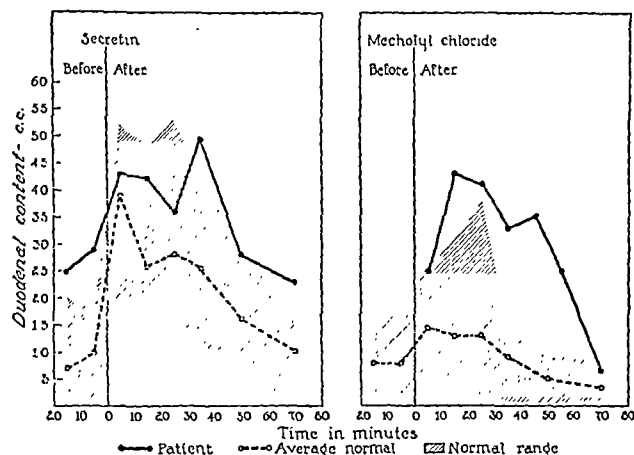


Fig. 2.—Large volume of duodenal content recovered per unit of time from a patient with chronic pancreatitis, after stimulation with secretin and with acetyl beta-methylcholine chloride, contrasted with the volumes obtained from normal persons.

obtained in this case are contrasted with the extremes as well as the means obtained in normal persons, demonstrate a hypersecretion of the pancreatic juice (fig. 2), a normal increase in values for hydrogen ion concentration but a marked hyposecretion of amylase. The values for concentration of amylase did not exhibit the typical decrease in concentration consistently seen in the second ten minute period (fig. 3) nor did the total values for amylase exhibit the usual marked increase during the first ten minute period (fig. 4). There was, in contrast, a hypersecretion of trypsin and lipase. Ågren, Lagerlöf and Berglund⁹ have called attention to the frequency with which pancreatic injury causes a marked reduction in secretion of amylase without interfering with the secretion of fluid, bicarbonate or trypsin and suggested that this represents the mildest form of injury in pancreatitis. Chiray and Bolgert⁶ recognized both a dissociated trypsin and a lipolytic insufficiency. In those cases in which obstruction of the pancreatic duct or destruction of pancreatic tissue occurs, as in cases of carcinoma or fibrosis of the pancreas, there is a decrease in the volume of secretion and the secretion of all the enzymes may be affected in proportion to the destruction of tissue and the degree of obstruction of the duct. Secretin used as a stimulant of pancreatic secretion should prevent the occurrence of false low total values and should disclose the more marked disturbances of secretion of fluid, alkali and the three enzymes. However, inspection of figures 3, 4 and 5 shows that mild reduction of values will not become apparent because of the variations in normal values among normal persons. While the number of published reports of tests in proved pathologic states of the pancreas is relatively small, these as well as my own experiences with the test leave little doubt

in my own mind concerning the value of secretin for clinical study of the secretion of fluid, carbonate and enzymes by the acinar cells.

Drugs Which Stimulate the Vagus Mechanism: Pilocarpine, acetylcholine, acetyl beta-methylcholine chloride, physostigmine and prostigmine have all been used to stimulate pancreatic secretion. These drugs produce a secretion rich in enzymes and in this respect their action is similar to that of stimulation of the vagus nerve in animals. Osterberg and I⁸ have used the two barrel gastroduodenal tube, continuous suction and acetyl beta-methylcholine chloride administered subcutaneously in doses of 15 mg. to obtain a picture of the type of secretory response obtained. Following stimulation with mecholyl chloride (acetyl beta-methylcholine chloride) a small increase in volume occurs; there is no significant change in the hydrogen ion concentration but there is an increase in the concentration of enzymes which is prolonged in duration. The total values for the several enzymes per unit of time increase for thirty minutes or longer and appear to be due to an actual increase in the secretory output of enzymes. Contrasting effects of secretin and mecholyl chloride are well illustrated in figures 2, 3 and 4, which show the extremes as well as the means for the several values obtained from normal persons.

In the case of pancreatitis already presented in abstract form, external pancreatic secretion was also studied after stimulation with mecholyl chloride. Analysis of duodenal content after administration of this drug demonstrated a hypersecretion of fluid (fig. 2), a marked insufficiency of secretion of amylase (figs. 3 and 4) but a hypersecretion of trypsin and lipase, as was the case after secretin. The same dissociation of enzymatic insufficiency that occurred after stimulation with secretin is likewise seen when using mecholyl chloride as a stimulant. A generalized reduction below the normal range of values for volume of fluid and of enzymes occurs after stimulation with mecholyl chloride in cases

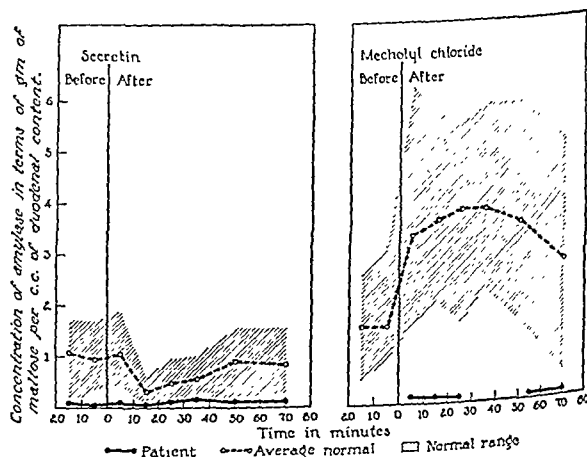


Fig. 3.—Low concentration of amylase in the duodenal content recovered per unit of time from a patient with chronic pancreatitis, after stimulation with secretin and with acetyl beta-methylcholine chloride, contrasted with the concentrations obtained in the duodenal contents recovered from normal persons.

of obstruction of the pancreatic duct and in cases of destruction of the acinar cells. Diminution of concentration as well as in total output of enzymes may give some inkling of pancreatic insufficiency. Drugs of this group and particularly mecholyl chloride should be valuable in the study of secretion of enzymes but are of

9. Ågren, Gunnar; Lagerlöf, Henrik, and Berglund, Hilding: The Secretin Test of Pancreatic Function in the Diagnosis of Pancreatic Disease, *Acta med. Scandinav.* 90: 224-271, 1936.

no value in studying secretions of carbonates. Foods are distinctly less powerful stimulants of pancreatic secretion than are either secretin or mecholyl chloride.

Analysis of Stools for Enzymes.—Amylase and trypsin are normally present in the feces. Lipase usually cannot be detected. Wolfer and Christian¹⁰ have pointed out that the amylase in the stools varies from day to day depending on the intake of food, and if the test is to be used clinically it can be effective only if the patients are placed on a uniform quantitative and qualitative diet. Even when using twenty-four hour specimens there is no constant relation between the amounts of amylase either of patients on the same diet or of the same persons from day to day, although the weekly totals approximate one another closely. Decreased values for fecal amylase occur in cases of obstruction to the duct and in extensive disease of the pancreas.^{10a} Wolfer and Christian do not feel that mild involvement of the pancreas can be confirmed by determinations of fecal amylase.

Examination of the stools for enzymes has not proved to be a popular method for study of external pancreatic function for obvious reasons.

Analysis of Stools for Undigested and Unabsorbed Food.—Many observations have shown that all food-stuffs are lost in excess in the presence of pancreatic disease and have led to the gross and microscopic examination of the stools and chemical examination of the stools for undigested foods as aids in the diagnosis of chronic pancreatic disease.

Gross Appearance of Feces: The excessive loss of fat in the stools lends the characteristic appearance to the stools of pancreatic disease. Fat may be lost in the form of neutral fat, fatty acids or soap. A fatty stool may be glistening white or gray. Fat may appear as liquid fat or as masses of fat resembling butter. Fatty crystals may give the feces the appearance of aluminum paint. According to Thaysen,¹¹ the only form of steatorrhea which is characteristic of pancreatic disease is that in which liquid fat or masses of fat appear in the stools.

Microscopic Examination of Feces: A description of the microscopic method of examination may be found in any standard textbook on laboratory diagnosis. An excess of all food remnants may appear in the feces from excessive ingestion as well as from deficient digestion and absorption. For this reason it is preferable to carry out microscopic examinations of the stools only when patients are receiving a standard test diet, such as that of Schmidt. It is doubtful that finding microscopically any foodstuff in excessive amounts is diagnostic of pancreatic disease, as such tests of necessity must be qualitative. The finding of striated muscle fibers in excess possibly has more significance than the finding of starch granules and fat in excess, but it is best to let such observations serve as an indication for more specific tests of pancreatic function and not depend on them to diagnose the cause of the loss of food.

Chemical Analysis of Feces: In carrying out chemical analysis of the stools, the patient is placed on a

standard diet such as that of Schmidt. In persons with normal digestive apparatus, digestion and absorption is fairly complete; the values for nitrogen, carbohydrate and fat in the stools seldom exceed 10 per cent of the values for nitrogen, carbohydrate and fat in the ingested food but vary somewhat with the digestibility of the food eaten. All foods are lost in excess when extensive destruction of the acinar cells of the pancreas has occurred.

Thaysen's review of the percentages of various foods lost in the feces in his own cases and in those recorded in the literature leads to the conclusion that such determinations would possibly be of limited value in distinguishing between pancreatic disease and diseases that affect intestinal absorption.

TESTS FOR DISTURBANCES OF THE "INTERNAL" SECRETION OF ACINAR CELLS

The enzymes lipase and amylase normally are active to a slight degree in the blood stream. Tryptic activity in the blood stream is said to be absent in normal per-

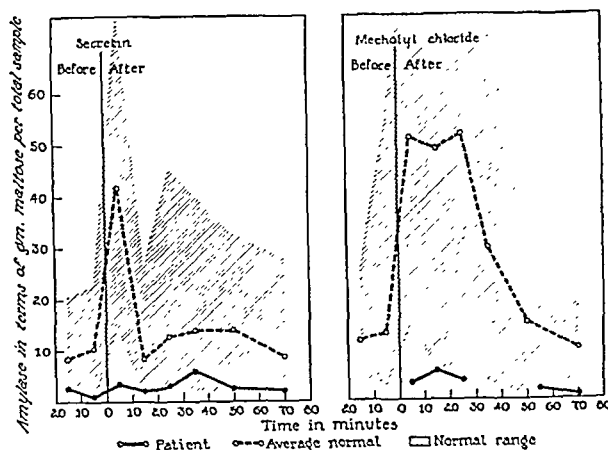


Fig. 4.—Total amount of amylase in the duodenal content recovered per unit of time from a patient with chronic pancreatitis, after stimulation with secretin and with acetyl beta-methylcholine chloride, contrasted with the total amount obtained in the duodenal contents recovered from normal persons.

sons but this enzyme has not been studied widely. Satisfactory evidence that the enzymes lipase and amylase arise partly in the pancreas may be cited; this may mean that they are in part at least an internal secretion of the pancreas, but it is not known whether they enter the blood stream directly from the acinar cells or indirectly from the gastrointestinal tract. Nevertheless, classification of values for enzymes in serum and urine as tests of internal secretion of the acinar cells is open to criticism; however, it is convenient to do so and serves to emphasize that the increased content of enzyme in the serum and urine in the presence of benign and malignant lesions of the pancreas originates in the acinar cells of the pancreas.

The factors which maintain the normal concentration of enzymes in the serum in health are not well understood. It is believed that the liver plays a role¹⁴ and that the anterior lobe of the pituitary gland,¹⁵ the thy-

10. Wolfer, J. A., and Christian, L. W.: Pancreatic Function Tests with Special Reference to the Quantitative Determination of Fecal Amylase. *Arch. Surg.* **17**: 899-917 (Dec.) 1928.

10a. McClure, C. W., and Pratt, J. H.: A Study of the Diastatic Activity of Urine and Feces with Special Reference to Diseases of the Pancreas. *Arch. Int. Med.* **19**: 568-592 (April) 1917.

11. Thaysen, T. F. H.: Ueber Fettdiarrhöen. *Acta med. Scand.* **64**: 292-400, 1926. On Steatorrhea, *ibid.* (suppl.) **16**: 384-396, 1926; Pancreatogenous Fatty Diarrhea: Report of Case. *Arch. Int. Med.* **42**: 352-367 (Sept.) 1925.

14. Crandall, L. A., Jr., and Cherry, I. S.: The Regulation of Blood Lipase and Diastase by the Liver. *Am. J. Physiol.* **97**: 515-516 (June) 1931. Somogyi, Michael: Blood Diastase as an Indicator of Liver Function. *Proc. Soc. Exper. Biol. & Med.* **32**: 538-540 (Dec.) 1934.

15. Cope, O., and others: Endocrine Function and Amylase Activity: Further Observations of Blood Serum Amylase Activity in Relation to Pituitary, Pancreas and Thyroid Function in Dog and Rabbit. *Endocrinology* **25**: 248-256 (Aug.) 1939.

roid gland¹⁶ and the adrenal gland¹⁷ exert some influence. The elevated values for enzymes which occur experimentally and clinically in inflammatory disease of the pancreas and in experimental and clinical obstruction of the pancreatic duct presumably have occurred as a result of rupture of small pancreatic canaliculi permitting entrance of pancreatic juice into the blood stream, perhaps through the lymphatic vessels, but it is also possible that irritative lesions of the acinar cells provoke a hypersecretion with increased values while destruction of the acinar cells prevents the appearance of increased values.

Determination of Values for Lipase and Amylase in the Serum.—Measurement of lipolytic and amylolytic activity can be accomplished by either physical or chemical methods. Among the methods available, those recently described by Cherry and Crandall¹⁸ for the determination of lipolytic activity and by Somogyi¹⁹ for the determination of amylolytic activity in the serum have been proved satisfactory. The simple titration method of Cherry and Crandall uses olive oil as the

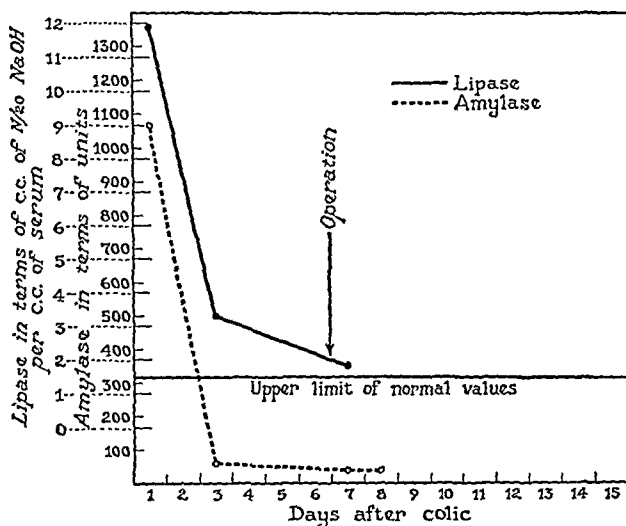


Fig. 5.—The behavior of concentrations of lipase and of amylase in the serum in cases of acute pancreatitis; the concentration of amylase usually returns to normal levels earlier than that of lipase.

substrate and it expresses lipolytic activity in terms of cubic centimeters of twentieth-normal sodium hydroxide liberated by 1 cc. of serum. The method of Somogyi employs iodine to measure the rate of disappearance of starch, and the values are defined in terms of units. Osterberg and I²⁰ have found it advisable to use 1.5 cc. of twentieth-normal sodium hydroxide and 320 units as the upper limits, respectively, for lipolytic and amylolytic activity in the serum. These values are considerably higher than those originally proposed for the upper limit of values for normal persons.

Elevated values in the serum occur within a few hours after the onset of acute inflammation of the pancreas,²¹ reaching a maximum within forty-eight to seventy-two hours (fig. 5). Elevated values for lipase usually return to normal within ten to fourteen days but elevations may persist over a long period of time; thus, elevated values for lipase have been obtained in every determination made over a period of months in the case of chronic pancreatitis reported herein. On the other hand, elevated values for amylase in the serum usually return to normal within a week,²² often earlier, although elevated values following experimentally produced pancreatitis have been found to persist as long as from eight to fifteen days.²³

Elevated values occur with great frequency in association with pancreatitis without associated disease of the biliary tract and in cases of pancreatitis secondary to disease of the biliary tract, provided the determinations are carried out within a few days after an acute attack of upper abdominal pain or during the acute stage of obstruction of the pancreatic duct. Osterberg and I²⁰ have laid down rigid criteria to be used in the interpretation of results in a recent analysis of our data. We expected elevated values in every case in which pancreatitis was described by the surgeon as subacute or acute, with or without fat necrosis, or as extensive (graded 3 to 4 on the basis of 4), provided determinations were carried out within seven to ten days of an acute attack of upper abdominal pain or, in other words, within the times during which elevated values could reasonably be expected. In these cases in which the pancreatitis was assumed to be active and acute, elevated values for lipase were obtained in 97 per cent of cases; a single low normal value occurred in a case of hemorrhagic pancreatitis in which a failure of values for lipase to increase was attributed to rapid and complete disintegration of the pancreas with destruction of the lipase producing tissue. More important, the condition of the pancreas was accurately indicated in 97 per cent of cases of disease of the biliary tract in which the condition of the pancreas was described by the surgeon.

The percentage accuracy of the determinations of amylase in the serum in the diagnosis of active pancreatitis was not quite so great as that of lipase, but this is probably due to the more rapid return of values for amylase to normal following an acute attack. Increased values for amylase and lipase in the serum have likewise occurred in cases of pancreatitis secondary to perforating benign and malignant lesions of the stomach and duodenum.²⁴ Increased values for lipase serum have been reported in 40.5 per cent of cases of carcinoma of the head of the pancreas, whereas those for amylase occur in only 8 to 22 per cent.²⁵ Elevated values have occurred in about 10 per cent of cases of hepatic disease, whereas elevated values for amylase

16. Bartlett, Willard Jr. (introduced by M. Somogyi): Effects upon Blood Amylase of Variations in Thyroid Activity, *Proc. Soc. Exper. Biol. & Med.* **36**: 843-848 (June) 1937.

17. Cope, O., and others. Endocrine Function and Amylase Activity: Changes in Activity of Blood Serum Amylase in Response to Changes in Adrenal Cortical Function in the Dog and Rabbit, *Endocrinology* **25**: 236-247 (Aug.) 1939.

18. Cherry, I. S., and Crandall, L. A., Jr. The Specificity of Pancreatic Lipase: Its Appearance in the Blood After Pancreatic Injury, *Am. J. Physiol.* **100**: 266-273 (April) 1932. Comfort, M. W., and Osterberg, A. E.: Lipase and Esterase in the Blood Serum: Their Diagnostic Value in Pancreatic Disease, *J. Lab. & Clin. Med.* **20**: 271-278 (Dec.) 1934.

19. Somogyi, Michael: Micromethods for the Estimation of Diastase, *J. Biol. Chem.* **125**: 399-414 (Sept.) 1938.

20. Comfort, M. W., and Osterberg, A. E.: The Value of Determination of the Concentration of Serum Amylase and Serum Lipase in the Diagnosis of Disease of the Pancreas, *Proc. Staff Meet., Mayo Clin.* **15**: 427-432 (July 3) 1940. Comfort.²⁶

21. Elman, Robert: The Variations of Blood Amylase During Acute Transient Disease of the Pancreas, *Ann. Surg.* **105**: 379-384 (March) 1937. Comfort.²⁷

22. Elman, Robert: Diagnosis and Treatment of Acute Nonhemorrhagic Pancreatitis, *Am. J. Digest. Dis. & Nutrition* **4**: 732-736 (Jan.) 1938.

23. McCaughan, J. M.: The Value of Estimations of the Amylase of the Blood in the Diagnosis of Suspected Pancreatic Disease: An Experimental Study and Review of the Literature, *Surg., Gynec. & Obst.* **59**: 598-609 (Oct.) 1934.

24. Probst, J. G.; Wheeler, P. A., and Gray, S. H.: Perforated Peptic Ulcer: Its Differentiation from Acute Pancreatitis by Blood Diastase Determination, *J. Lab. & Clin. Med.* **24**: 449-452 (Feb.) 1939. Comfort.²⁸

25. Wakefield, E. G.; McCaughan, J. M., and McVicar, C. S.: Amylase in the Blood in Subacute and in Chronic Pancreatic Diseases, *Arch. Int. Med.* **45**: 473-478 (March) 1930. Comfort.²⁹

have not been reported in disease of the liver.²⁶ No good reason has so far been advanced for believing that these or other elevations are due to causes other than involvement of the pancreas by a disease. In short, elevated values occur in association with benign and malignant obstruction of the pancreatic duct and with inflammation of the pancreas situated primarily in the organ or involving it secondarily from diseases in the neighboring organs.

Determination of Values for Amylase in the Urine.—It is accepted that amylase in the urine is derived from the blood, that a rise in urinary diastase occurs within one to two hours after an acute attack of pancreatitis begins and shortly after the rise in blood amylase, and that the increase lasts from thirty-six to forty-eight hours and then falls suddenly and is usually normal in from three to four days. Elevations occur also during exacerbations of chronic pancreatitis. Renal damage may interfere with the excretion of amylase. Elevated values occur in cases of acute pancreatitis unassociated with disease of the biliary tract, in cases of acute pancreatitis secondary to disease of the biliary tract and duodenal ulcer penetrating into the pancreas, but rarely in cases of carcinoma of the pancreas. Wohlgemuth's original method or some modification of his method has usually been used for the determination of amylolytic values in the urine. Somogyi's method has gained favor recently.

Determinations of amylase in the urine as a test of disturbance of internal secretion of the acinar cells has been widely used for many years²⁷ and many conflicting opinions about its accuracy in the diagnosis of pancreatic disease have been expressed. As one reads the reports of the various investigators, the thought arises that the discouraging reports of early investigators were possibly due to ignorance of the relatively short duration of elevations of values following an acute attack and the lack of knowledge of the milder degrees of pancreatitis, and that elevated values previously thought due to cholecystitis and common duct stone were probably for the most part due to pancreatitis of a mild degree associated with the disease of the biliary tract, a type of pancreatic inflammation not widely recognized at the time when the studies were made.

It may be accepted, for the present, that elevated values for lipase and amylase in the serum and for amylase in the urine usually point to disease of the pancreas; that the pancreatic disturbance may be primary in the pancreas or secondary to disease of the biliary tract, to benign or malignant disease of the stomach, to duodenal ulcer or even to stasis in the pancreas; that determinations of the concentrations of enzymes do not allow for a diagnosis of the type of pancreatic disease nor do they serve to indicate the severity of the process; that normal values do not rule out pancreatitis since normal values may be obtained when extensive destruction of the acinar cells has occurred; that clinical symptoms and clinical signs must be used in conjunction with these tests in arriving at a clinical diagnosis of the type of disease that is present in the pancreas.

The determinations both of lipase and of amylase in the serum have their own advantages. Thus, amylase determinations can be done within the hour while that for lipase requires twenty-four hours. On the other

hand, elevated values for lipase are associated more frequently with malignant disease of the pancreas than are elevated values for amylase, and the elevations for lipase in acute inflammation of the gland persist for a longer period of time than do elevated values for amylase. Elevated values for lipase in association with hepatic disease sometimes may confuse the diagnosis, but this should not be the case if the elevations in the value for this enzyme are always interpreted in the light of historical, clinical and other laboratory data.

TESTS FOR DISTURBANCES OF INTERNAL SECRETION OF ISLANDS OF LANGERHANS

Disturbed Secretion of the Hormone of Carbohydrate Metabolism.—The hormone insulin, concerned in carbohydrate metabolism, is probably secreted by the beta cells of the islands of Langerhans, and tests for disturbance of its secretion in common use in the diagnosis of diabetes mellitus may also be used in the study of disturbances of this secretion in the presence of other diseases of the pancreas. Glycosuria has been reported in from 5 to 20 per cent of cases of acute pancreatitis²⁸ and occurred more frequently in the severe cases. Hyperglycemia has been encountered in 50 per cent or more of the cases of acute pancreatitis²⁹ and occurred more frequently in pancreatic necrosis than in acute pancreatic edema. Bernhard³⁰ has expressed the opinion that the test for dextrose tolerance will disclose a disturbance of carbohydrate metabolism in a high percentage of cases of acute pancreatic disease in which glycosuria and hyperglycemia are absent. He also has said that the test for dextrose tolerance discloses mild disturbance of carbohydrate metabolism in the presence of pancreatic edema and discloses severe disturbances in cases of pancreatic necrosis. The test thus serves to distinguish between the two types of acute pancreatic disease. From these reports it would appear that, if preexisting diabetes can be excluded, glycosuria, hyperglycemia and disturbed tolerance for dextrose should point definitely to pancreatic inflammation if found during an attack of upper abdominal pain. However, in view of the readiness with which glycosuria, disturbances of concentrations of sugar in the blood and disturbances of tolerance for dextrose occur in association with infections, in attacks of cholecystitis and even in coronary thrombosis,³¹ fasting concentrations of sugar in the blood (less than from 175 to 200 mg. per hundred cubic centimeters) and tests showing disturbance of tolerance for dextrose should be interpreted with extreme conservatism.

Tests for Disturbed Secretion of the Hormone Concerned in the Metabolism of Fat.—A depancreatized dog maintained on a balanced diet and insulin eventu-

26. Comfort, M. W.: Serum Lipase: Its Diagnostic Value, *Am. J. Digest. Dis. & Nutrition* 3: 817-821 (Jan.) 1937.

27. Foged, Jens: The Diagnostic Value of Urine Diastase, *Am. J. Surg.* 27: 439-446 (March) 1935. Mushin, M.: Urinary Diastase in Acute Pancreatitis, *Australian & New Zealand J. Surg.* 2: 133-140 (Oct.) 1932. Schmieden, V., and Sehening, W.: Chirurgie des Pankreas, *Arch. f. klin. Chir.* 148: 319-387, 1927. McClure and Pratt.¹

28. Beckman, T. M.: Contributions au diagnostic des pancréatites chirurgicales, *Acta chir. Scandinav.* (suppl. 44) 78: 1-328, 1936. Henderson, F. F., and King, E. S. A.: Acute Pancreatitis, *Arch. Surg.* 30: 1049-1057 (June) 1935. Love, R. J. M.: Acute Pancreatitis: Clinical Features and Treatment, *Lancet* 2: 1262-1264 (Dec. 18) 1926. McWhorter, G. L.: Acute Pancreatitis: Report of Sixty-Four Cases, *Arch. Surg.* 25: 958-990 (Nov.) 1932. de Takats and Mackenzie.²⁹ Rosenberg.²⁹

29. Rosenberg, Max: Funktionsstörungen des Inselapparates bei akuten Pankreatitis, *Klin. Wchnschr.* 10: 917-920 (May 16) 1931. de Takats, Geza, and Mackenzie, W. D.: Acute Pancreatic Necrosis and Its Sequelae, *Ann. Surg.* 96: 418-440 (Sept.) 1932. Brocq, P., and Varangot, J.: L'hyperglycémie dans les pancréatites aiguës: Sa valeur au point de vue du diagnostic, du pronostic et du traitement, *Bull. et mém. Soc. nat. de chir.* 60: 25-32, 1934. Casberg, M. A.: Acute Pancreatic Necrosis and Acute Interstitial Pancreatitis: Treatment Without Operation: A Clinical Study of Ten Cases, *Arch. Surg.* 39: 247-263 (Aug.) 1939. Trasoff, Abraham, and Scarf, Maxwell: Acute Pancreatitis: A Medical Problem, *Am. J. M. Sc.* 104: 470-474 (Oct.) 1937.

30. Bernhard, F.: Der Wert von Blutzucker- und Diastasebestimmungen für die Diagnostik, Operationsindikation und Nachbehandlung der akuten Pankreaserkrankungen, *Klin. Wchnschr.* 9: 1346-1351 (July 19) 1930.

31. Raab, A. P., and Rabinowitz, M. A.: Glycosuria and Hyperglycemia in Coronary Thrombosis, *J. A. M. A.* 106: 1705-1708 (May 16) 1936.

ally experiences hypolipemia and marked fatty metamorphosis together with impaired function of the liver, diminished excretion of dextrose and a marked sensitivity to insulin. In 1936 Dragstedt, van Prohaska and Harms³² presented evidence that these changes were due to a deficiency of a hitherto undescribed internal secretion manufactured by the pancreas. They suggested the name "lipocaic" for this substance, which they assumed had to do in a general way with utilization of fat and they prepared an extract of the pancreas that would reverse these changes in the liver and increase the concentration of blood fats. Ivy and Gray³³ in 1939 concluded, however, after a review of the facts pro and con, that the evidence supporting the view that lipocaic is an internal secretion of the pancreas is by no means complete but that the evidence that lipocaic is not choline and that it is effective in preventing a deposition of fat in the liver of depancreatized dogs is very convincing. The experiments of Bensley and Woerner³⁴ would indicate that the alpha cells of the islands of Langerhans secrete the substance concerned with fat metabolism. Reports indicate that deficiency of the secretion of the hormone dealing with metabolism of fat has been encountered in cases of pancreatitis and among diabetic patients.³⁵ In these cases, bromsulphalein and hippuric acid tests have disclosed disturbances of hepatic function. Changes in blood cholesterol levels have also been observed.

COMMENT

We may safely conclude that tests exist whereby the functions of the different types of cells of the pancreas may be adequately studied.

The determination of the volume of duodenal content, its p_H values, the concentration and total excretion of bicarbonate and enzymes per unit of time after stimulation of the pancreas with purified secretin and mecholyl chloride, all constitute an especially promising group of tests of external function of acinar cells and are especially useful in cases of pancreatitis after the acute phase has passed, in cases of chronic sclerosing pancreatitis and malignant disease of the pancreas.

Measurement of the values for lipase and amylase in the serum and urine is very useful for detecting functional alterations of acinar cells due to either inflammation of the gland or obstruction of the pancreatic duct.

Determination of values for sugar in the urine and in the blood and of the tolerance for dextrose supplies trustworthy information about the secretory disturbances of the islands of Langerhans in cases of pancreatitis, provided that preexisting diabetes can be excluded.

It is emphasized that these tests are tests of pancreatic function. The results of such tests do not in themselves indicate the type or the degree of the pathologic change present in the pancreas. On the contrary, the type of pancreatic disease present and its degree of severity must be decided on the basis of the history, physical conditions and the results of other laboratory examinations.

32. Dragstedt, L. R.; Van Prohaska, John, and Harms, H. P.: Observations on a Substance in Pancreas (a Fat Metabolizing Hormone) Which Permits Survival and Prevents Liver Changes in Depancreatized Dogs, *Am. J. Physiol.* **117**: 175-181 (Sept.) 1936.

33. Ivy, A. C., and Gray, J. S.: Application of Recent Contributions in Basic Medical Sciences to Surgical Practice, *Internat. Abstr. Surg.* **69**: 1-7, 1939; in *Surg., Gynec. & Obst.*, July 1939.

34. Bensley, S. H., and Woerner, C. A.: The Effects of Continuous Intravenous Injection of an Extract of the Alpha Cells of the Guinea Pig Pancreas on the Intact Guinea Pig, *Anat. Rec.* **72**: 413-433 (Dec.) 1938.

35. Rosenberg, D. H.: Proved Case of Recovery from Fatty Metamorphosis of the Liver After Treatment with Lipocaic, *Am. J. Digest. Dis. & Nutrition* **5**: 607-613 (Nov.) 1938. Snell, A. M., and Comfort, M. W.: Hepatic Lesions Presumably Secondary to Pancreatic Lithiasis and Atrophy: Report of Two Cases, *ibid.* **4**: 215-218 (June) 1937.

STUDIES IN OLD AGE

IV. THE CLINICAL SIGNIFICANCE OF SALIVARY, GASTRIC AND PANCREATIC SECRETION IN THE AGED

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AND

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The digestion of the aged has received but little attention in the literature. There is, however, a common belief among the medical profession and the public that disturbances of digestion are associated with a faulty dietary, and restriction of diet and special diets have therefore been the vogue for the aged. Much of what is accepted seems to be based on fear and habit rather than on basic experimental observations.

It is also known that gastrointestinal symptoms are common in the aged while organic diseases of the gastrointestinal tract are relatively uncommon. According to Rivers,¹ indigestion is a complaint of half of the patients between the ages of 30 and 60, and Barker² and his associates have studied the case histories of 300 patients past 60 years of age and noted that digestive symptoms were second highest in frequency; they found that despite the high incidence of digestive symptoms in this group there were only three cases of gallbladder disease, two of ulcer of the pylorus and two of ulcer of the duodenum. It is generally recognized that, in the aged, gastrointestinal symptoms may often be due to diseases outside the alimentary tract, as for example cardiac, renal, arthritic and hematologic disease.

Digestive disturbances, however, which may result from physiologic changes in the gastrointestinal tract, accompanying the aging process, are not clearly defined.

Observations in Two Age Groups

Age		Basal Secretion				Stimulated Secretion			
		Ptyalin Concentration				Ptyalin			
Years	Average	Number of Subjects	Variation	Average	Volume, Cc.	Average	Variation	Average	Specific Gravity
21-31	25	12	2.4-22.2	10.15	13.6-15	14.2	2.14-3	8.2	1.001
60-100	81	27	0.19-0.48	0.303	1.5-15	5.8	0.18-0.42	0.28	1.009

We therefore undertook a study of the secretion of the aged in order to establish what is normal and also to clarify the relationship which may exist between the secretory changes in the aged and clinical symptoms.³

We studied the basal (fasting) secretion of saliva and the secretion of saliva after a stimulus (chewing). Chart 1 illustrates the basal secretion of salivary amylase in thirty-two persons from 12 to 60 years of age and in twenty-nine persons from 60 to 90 years of age.⁴ The results in part A of chart 1 demonstrate the forma-

Aided by a grant from Mr. John Gottlieb.

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1. Rivers, A. B.: The Dangers of Treating "Indigestion" by Adversified Nostrums, *Proc. Staff Meet., Mayo Clin.* **13**: 87 (Feb. 9) 1938.

2. Barker, L. C., in Cowdry, E. V.: Problems of Ageing, Baltimore, Williams & Wilkins Company, 1939, p. 717.

3. Meyer, Jacob: The Management of Diseases of the Gastrointestinal Tract in the Aged, *M. Clin. North America* **9**: 21 (Jan.) 1940.

4. Meyer, Jacob; Spier, Ernst, and Neuwelt, Frank: Basal Secretion of Digestive Enzymes in Old Age, *Arch. Int. Med.* **65**: 171 (Jan.) 1940.

tion of maltose from starch (end point method) and in part B the formation of dextrin from starch by salivary amylase. The latter method shows the intermediary products of digestion of starch by saliva, and the results obtained are of importance because only part of the starch ingested is digested completely (i. e. to maltose) in the mouth and stomach. The results demonstrate that the conversion of carbohydrates by salivary amylase to maltose and dextrin is markedly depressed in the aged, and particularly the formation of dextrin. Thus the first stage of starch digestion is severely depressed while complete digestion of starch is considerably diminished. This confirms previous work⁵ in which volume, and ptyalin content of stimulated salivary secretion was investigated, only the Wohlgemuth method (dextrin) being used.

The values found in this work were lower than those reported before, but different groups of subjects were employed, of different stock and on different nutrition. We are therefore of the opinion that there is a marked

in younger persons, occurring mainly after stimulation by a meal.

Our conclusion from this study is that in old people carbohydrate digestion is probably completed in the intestinal tract and that the pancreatic amylase is a substitute for the salivary amylase.

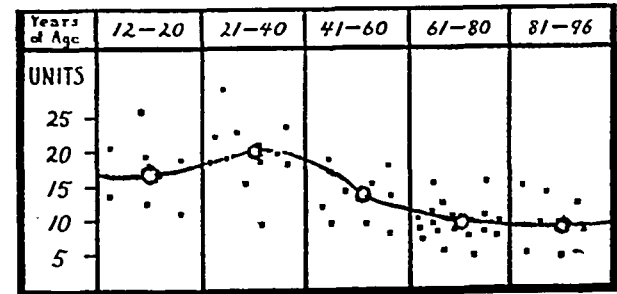


Chart 2.—Pancreatic amylase. This graph is rather similar to chart 1 A, except that the units are much less. It is obvious from the chart that the aged need suffer no embarrassment of carbohydrate digestion.

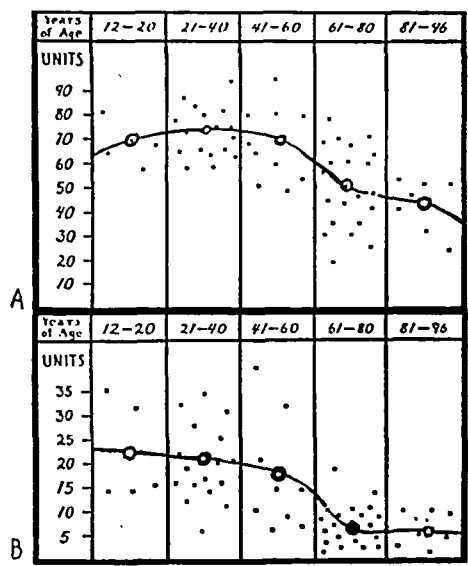


Chart 1.—A, salivary ptyalin estimated by the Shaw and Ross method. The enzyme activity falls little in the older age groups, although a downward trend is evident. The reaction is carried to completion, i. e. to the formation of maltose. B, salivary ptyalin estimated by the Wohlgemuth method. The concentration of ptyalin falls markedly about the sixtieth year of life. This reaction involves only the first step in the breakdown of starch to achroodextrin (amylolastic action).

decrease or incomplete digestion of carbohydrates in the mouth and to a certain degree in the stomach of old people. Old people eat a considerable amount of carbohydrate foods because they are easier to chew and because in institutions for the aged carbohydrates comprise a greater portion of the diet. We expected to find evidence of incomplete carbohydrate digestion. It is of interest, however, that old people seldom complain of symptoms indicating incomplete carbohydrate digestion. These clinical observations are explained by our later investigations⁶ in which we studied the pancreatic secretion of old people and discovered that stimulated pancreatic amylase is present in normal amounts while the amylase in the fasting duodenal juice is lower than in young people. This fact seems to indicate that in old people pancreatic secretion is more intermittent than

The dry tongue of old age may be explained by the decreased quantity of salivary secretion. The diminution of body fluids and the changes in blood chemistry may likewise be an important factor.

The tongue of the aged is often a difficult problem from a diagnostic and therapeutic aspect. It is important to differentiate the dry tongue due to metabolic disturbances and that due to such clinical entities as the anemia of the aged, achlorhydria, vitamin deficiency, Plummer Vinson's syndrome, pernicious anemia and psychogenic factors. Ivy⁷ states that the atrophic changes of the mucosa of the tongue are more frequent in the elderly people with achlorhydria than in those with gastric acidity.⁸ According to Hutter and Middleton⁹ the atrophic changes of the tongue are more related to dietary deficiency than to achlorhydria. It is very likely that both achlorhydria and diet are involved.

It has been established by numerous investigations that the incidence of achlorhydria increases with advancing age. There is much discussion as to whether

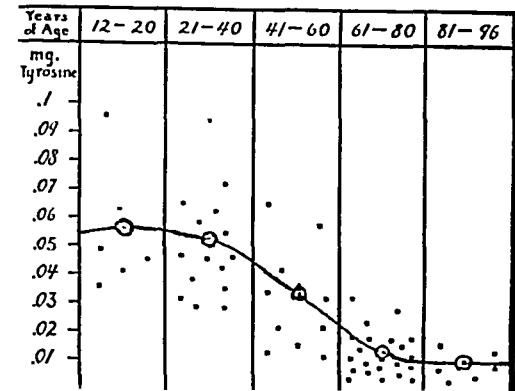


Chart 3.—Pepsin. The concentration falls sharply during the seventh decade of life and after that maintains a rather constant low value.

achlorhydria is due to a chronic gastritis, to an inherited predisposition or to a physiologic involution associated with senile atrophy. We determined the values for free

5. Meyer, Jacob; Golden, J. S.; Steiner, N., and Necheles, Heinrich: The Ptyalin Content of Human Saliva in Old Age, *Am. J. Physiol.* **119**: 600 (July) 1937.

6. Meyer, Jacob; Plotke, F.; Neuwelt, Frank, and Necheles, Heinrich: Studies on Old Age: A Comparison of the Secretion of the Pancreas in Old and in Young Subjects, unpublished.

7. Ivy, A. C., in Cowdry: *Problems of Ageing*, pp. 97, 1938.

8. Davies, D. T., and James, T. G. I.: Investigation into Gastric Secretion of 100 Normal Persons Over Age of 60, *Quart. J. Med.* **23**: 1 (Oct.) 1930.

9. Hutter, A. M., and Middleton, W. S.: Vitamin B Deficiency and the Atrophic Tongue, *J. A. M. A.* **101**: 1305 (Oct. 21) 1933.

acid in the fasting gastric juice of twenty-nine patients between the ages of 60 and 96. In approximately 65 per cent of these aged subjects there was no free acid in the fasting contents, while in 35 per cent of the younger subjects there was also no free acid in the fasting contents. We likewise made determinations of

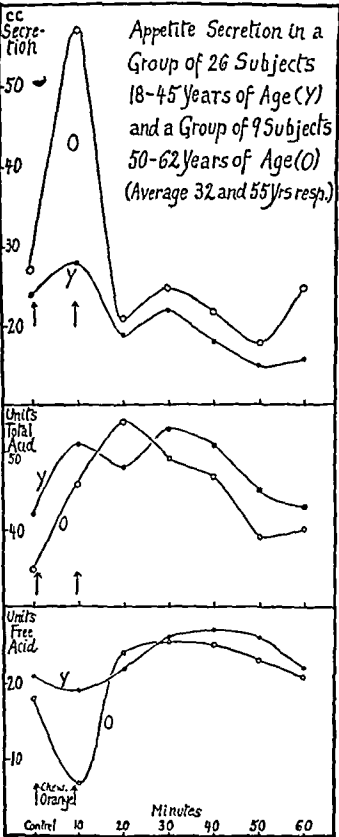


Chart 4.—Appetite secretion in a group of twenty-six subjects from 18 to 45 years of age (Y) and a group of nine subjects from 50 to 62 years of age (O), average 32 and 55 years respectively.

the secretion of pepsin decreased in age as much as does the secretion of acid.

In view of the importance of psychic secretion of the stomach for appetite and digestion it is of interest to see whether this is changed in old people. The data obtained in previous work by one of us¹¹ were therefore regrouped and charted according to age and are presented in chart 4. It shows that the free acidity of gastric juice following the chewing of chilled orange (nothing was swallowed) drops considerably in the old people ten minutes after stimulation, while in the younger group it rises at the same interval. After that both curves rise and the two are similar. The total acidity is roughly the same in the two groups, only slightly lower in the older people. The drop in free acidity is explained by greatly increased volume of secretion in the older group ten minutes after stimulation. This shows that the drop in free acidity was due to dilution by a fluid containing combined but no free acid.

The concentration of trypsin in our study is similar to that of pancreatic amylase. The fasting duodenal contents show a decidedly lower level in the aged, while

the concentration of pepsin. We found a steady drop in the concentration of pepsin during the seventh decade of life, and after that age the concentration maintained a constant low value. We could find no correlation between the concentration of the acid and pepsin in the fasting gastric juice.

Chart 3 indicates the low values for pepsin in old people. It also demonstrates that in the younger group there is greater variability in the pepsin concentration than in the group of old persons, in which it is relatively constant. Osterberg, Vanzant, Alvarez and Rivers¹⁰ made an analysis of the gastric juice of 6,200 patients and our observations parallel theirs closely in that the values for pepsin fluctuate widely in the case of young persons. These authors also found that after an Ewald meal

the stimulated pancreatic juice has the same concentration of trypsin in the old as in the younger group.

In spite of the low concentration of pepsin and trypsin, nothing has been written about special difficulties of old people for the digestion of proteins. It is likely that tryptic and peptic digestion in the intestine and possibly in the stomach (regurgitation) is adequate to meet the requirements of a small protein intake. We are, however, aware that there are old persons whose protein intake is fairly large who have no difficulties of digestion.

Lipase in the fasting duodenal contents and in the stimulated pancreatic secretion was distinctly lower in the old group as compared to the younger group, the difference being approximately 20 per cent. In view of the biologic reserve in all secretion this may not mean impaired digestion of fats except possibly when too much fat is ingested at one time.

The restrictions in diet, particularly restrictions of protein which are often self imposed or imposed by an overanxious or overprotective physician or family, are perhaps unwarranted in the light of our observation. With few exceptions the majority of old people select both quantity and quality of their foods which satisfy their needs and tastes. The family physician will do well to allow the aged to follow this "natural selection." It may be that the aged, just as children and animals, select foods which their organism requires.

The secretory changes which we have observed may be attributed to a gastritis rather than to the normal involution of old age. This is a most difficult problem to answer definitely. We are aware that in many people there may be no secretory change. We are likewise aware that these secretory changes may occur without any symptoms. Bloomfield noted changes in secretion with advance in years in some patients, while in others it remained unaltered. These observations likewise do not offer a solution for the changes in secretion in one group as contrasted with the apparently normal state of the secretion in others. It is necessary to make combined gastroscopic studies and secretory studies in old people to elucidate this problem further. Schindler's observations on atrophic gastritis would seem to indicate that in the aged the secretory changes are associated

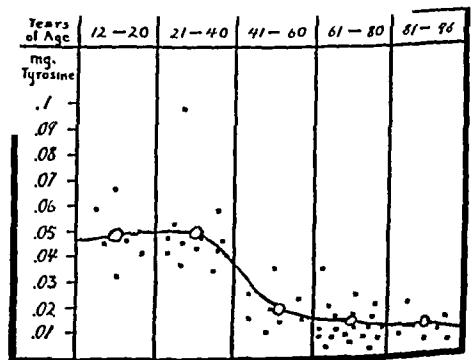


Chart 5.—Trypsin. The tryptic activity falls sharply after the fortieth year of life. The proteolytic powers of pancreatic juice bear no relation to gastric acidity.

with a gastritis. However, our own concept is that the process is probably an involutionary change.

It is possible that the quality of the food may be a factor in the secretory response. In deficiency diseases such as a vitamin B₁ deficiency there are changes in gastrointestinal secretions and motility. We therefore have made some preliminary observations on the rela-

10. Osterberg, A. E.; Vanzant, F. R.; Alvarez, W. C., and Rivers, A. B.: Studies of Pepsin in Human Gastric Juice, *Am. J. Digest. Dis. & Nutrition* 3: 35 (March) 1936.

11. Necheles, Heinrich, and Maskin, M. H.: Studies on Constitution and Peptic Ulcer: I. Appetite Secretion in Normal Persons and in Ulcer Patients, *Am. J. Digest. Dis. & Nutrition* 3: 90 (April) 1936.

tionship of vitamin B₁ to the achlorhydria of the aged.¹² We studied thirty-six patients between the ages of 52 and 80 who had achlorhydria to histamine and who presented no gastrointestinal symptoms; nor was there any evidence of vitamin deficiency to indicate that we were dealing with pellagra or pernicious anemia. Nine of these patients were given 15 mg. of thiamine hydrochloride hypodermically for fifteen days. No changes were observed in the free or total acidity as a result of this treatment. Nine patients were given 10 Gm. of brewers' yeast daily for a period of fourteen days and no notable change in free or total acidity was observed.

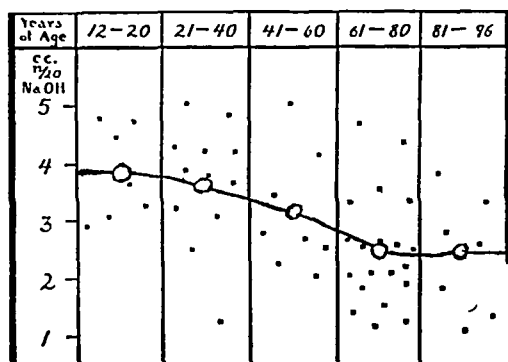


Chart 6.—Pancreatic lipase. The lipolytic activity of pancreatic juice is variable and is dependent neither on gastric acidity nor on the age of the subject.

The problem of appetite in the aged raises numerous questions. Carlson¹³ quotes Sternberg as saying that the "appetite is in some way associated with the tonus of the muscles of mastication and deglutition and the absence of appetite and the nausea is due to atony of these muscles." In the aged it is common to observe changes in the tonus of the musculature of the mouth, and appetite may be absent and nausea may or may not be a complaint. Carlson states that "a certain sensation complex from the viscera and a normal state of central correlation as a necessary background for appetite. Given this background the essential in appetite is the memory process of past experience, sight, smell and taste with palatable foods. These memories are reinforced by present stimulation of these nerves by food." Visual disturbances and changes which are said to occur in the taste buds and in the sense of smell in the aged may explain the absence or diminution of appetite in old people. Certainly the role of the memory process in the aged must be considered an important factor in relation to appetite. Additional factors, as the salivary and gastric secretion and the change in hunger contractions, undoubtedly play an important role in the appetite mechanism. It is important for the clinician to be familiar with the factors concerned in "appetite," particularly as it relates to old people. The older therapeutic measures such as wines, alcohol and bitters are said to be effective. Recent clinical experience shows that vitamin B is likewise of value in stimulating the appetite. While our observations indicate that vitamin B may not increase the gastric acidity in patients with achlorhydria, it may be effective in instances of lowered acidity, or again it is likely that vitamin B increases appetite by shortening the emptying time of the stomach.

12. Observations of Bernstein, Pearlman & Meyer, unpublished.
13. Carlson, A. J.: *The Control of Hunger in Health and Disease*, University of Chicago Press, 1916.

We wish to draw attention to the occurrence of acute peptic ulcer in the aged. It is generally believed that gastric and duodenal ulcer rarely occur in the aged and, if so, on the basis of arteriosclerosis of the gastric blood vessels. Our experience has been that ulcer is more frequent in the aged as a primary acute lesion than is generally recognized and that it is often present as a secondary disease, i. e. secondary to diseases of liver, kidney, heart or prostate. The general theory as to the genesis of ulcer presumes the presence of hyperacidity, but the relative frequency of achlorhydria or low values of acidity suggest that in the aged there may be other factors than the corrosive action of hydrochloric acid and pepsin responsible for the genesis of peptic ulcer. A gastritis in the aged as being an important factor in the etiology of ulcer is readily conceivable, because the diminution or absence of free acid permits the activity of bacteria to precipitate the ulcer process.

The frequency of perforation of peptic ulcer in the aged is also not readily explained. If the progress and activity of an ulcer are dependent on the digestive action of free hydrochloric acid and pepsin, one would expect fewer perforations because of the diminution of acid and enzymes. The occurrence of a fairly large percentage of perforations would indicate that there may be other factors which give rise to perforation in the aged.

SUMMARY

1. Gastrointestinal symptoms are common in old age, but gastrointestinal disease is relatively uncommon.
2. Old people show changes in the salivary, gastric and pancreatic secretion (except amylase), all of which are a decrease in the quantity of secretion and enzymes.
3. The diminution in the quantity of secretion apparently does not affect intestinal digestion.
4. Despite the diminution in the secretion, the secretory mechanism is capable of response under adequate stimulation.
5. Restrictions imposed on old people because of fear of inadequate digestion of carbohydrate, protein and fat do not appear warranted.
6. Acute peptic ulcer with severe complications occurs in old people in association with cardiac, renal, hepatic and prostate disease.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DR. COMFORT AND DRS. MEYER AND NECHIELES

DR. JOSEPH S. DIAMOND, New York: The older methods of studying the external secretion of the pancreas presented many difficulties. The use of food as a stimulus, the admixture of gastric chyme and the lowered pH values prevented one from obtaining accurate determinations of the functional activity of the gland. With the introduction of a purified secretin and the use of the double lumen gastroduodenal tube these difficulties have been overcome. Secretin is a potent pancreatic stimulus which is used parenterally in standard dosage. The separate collection of duodenal and gastric juices enables one to obtain a clear, uncontaminated pancreatic juice. The withdrawal of the juices under gentle suction supplies one with the total output of the secretion of the gland for a given time, for the complete quantitative study of the volume, alkalinity and the enzymes amylase, trypsin and lipase. The volume of pancreatic juice collected following the secretin injection varies between 135 and 250 cc. and is rich in bicarbonate and all the enzymes. Physiologically the secretion of the pancreas is controlled by a neuro-hormonal mechanism. The volume and bicarbonate are directly proportional to the hormone secretin, while the enzymes are dependent in addition to the vagal tone. When vagal stimulants

such as insulin and acetylcholine are used in conjunction with secretin the concentration of the enzymes is increased from two to three fold, while the volume and bicarbonate remain unchanged. Dr. Comfort has used mecholyl while I have used insulin, injecting 16 units intravenously one half hour before secretion. In pathologic states of the pancreas the enzymes become affected first, bicarbonate last of all. The enzymes may become dissociated so that one may be affected more than another. In severe lesions all functions are simultaneously affected. I have been working with secretin since 1938. Dr. Siegel and I have performed by now 130 tests in 104 individuals, of whom twenty-four were normal and eighty pathologic. The test has helped us to discover lesions of the pancreas in many instances in which it was least suspected. In cases of painless jaundice, with identical clinical pictures of obstructive jaundice, the test has helped us differentiate a carcinoma of the head of the pancreas from a primary lesion of the common bile duct. In acute hemorrhagic pancreatitis the test revealed a very marked depression in all the functions, showing but little recovery even as late as ten months after the operation. In a group of cases of steatorrhea we were able to differentiate the idiopathic forms from those having pancreatic disturbances.

DR. A. C. IVY, Chicago: I should like to commend Dr. Meyer and Dr. Necheles and their associates for the type of work they have been doing. The physiology of digestion of the infant and child has been placed on a sound basis by experimental and clinical investigation. In the field of geriatrics the physiology of digestion will be placed on a sound basis only by experimental and clinical investigation. Considerable information is available concerning the physiology of digestion in the infant, the child and the adult, but there is little information regarding that subject in the aged. If present population trends continue, the subject of geriatrics is likely to become as important as the subject of pediatrics is today. I should like to recommend that they continue their study on the enzymes to include studies on motor activity and then to study the coefficient of digestion of foods. The coefficient of digestion is the principal subject of interest. One should be interested not only in the enzymes that are secreted but also in the motor and the absorptive activity. By knowing the intake of protein, fat and carbohydrate and by analyzing the feces, one can determine the extent to which protein, fat and carbohydrate are being digested and absorbed. I should like to emphasize the importance of stool analysis. I have met gastro-enterologists who have forgotten the importance of stool analysis. When one performs the "new secretin" tests one should correlate the results with stool analysis. One should not be misled by the results of a study of the enzyme output of the pancreas, as occurred a number of years ago by a fractional study of the acidity of gastric contents, forgetting to study and pay close attention to the stools.

DR. EDWARD S. EMERY JR., Boston: It is a common experience to encounter elderly persons with gastrointestinal disturbances. The symptoms vary widely and are frequently similar to those accompanying organic disease in younger persons. Although it cannot be said that there are gastrointestinal symptoms of old age which are characteristic diagnostically, certain traits of behavior occur frequently enough to justify comment. Often the symptoms are intermittent, disappearing and returning for no apparent reason. Many notice a decreased appetite which their physicians attribute to a sedentary existence. Others find that their desire to eat is as good as formerly but that they are no longer able to take large meals without distress. With these patients the kind of food appears to be of less importance than the amount. Still others have a normal appetite for breakfast, whereas they have little desire for food the rest of the day. These patients find that their appetite is a good index of how well their stomach tolerates food. The "digestion" of old persons is influenced strongly by fatigue, which undoubtedly explains many of the apparent vagaries in the general behavior of their symptoms. This striking influence of fatigue would seem to be explained by the decreased enzymatic concentrations which are reported by Dr. Meyer and Dr. Necheles, because their studies suggest that the digestive ferments of the saliva and stomach are reduced in old age. Presumably the elderly cannot make secretions as rapidly as the younger person. It is interesting to know that the older pancreas responds to stimulation like the

younger one. I have just reported before the American Gastro-Enterological Association the results of some studies on the enzymes of the upper jejunum made at the Peter Bent Brigham Hospital during the past year. The striking lesson from these studies is the rapidity with which the enzymes regain their normal concentration after their equilibrium has been disturbed. There was some reason to believe that the pancreas might help to readjust this disturbance. The indigestion of age is explained better by a diminution in the amounts of enzymes secreted than by the sedentary existence of these patients. Also it may explain the greater susceptibility to physical fatigue of the older digestive tract. If digestion is adequate only for breakfast, this may be due to storage of digestive elements during the night, permitting a sufficient amount for this meal but an inability to make ferments fast enough to take care of the noon and evening meals.

DR. JOHN L. KANTOR, New York: May I emphasize what Dr. Ivy has said? The clinician, in studying the work of the pancreas, must investigate the stools for his final appraisal. A. J. Carlson voiced this thought about ten years ago, and five years ago it was stressed by Dr. Pratt of Boston. The secretion of the pancreas supplies three important ferments. As far as the amylase is concerned, it must be admitted that there is no clinically effective method of studying the result of carbohydrate digestion in the stool. When it comes to the work of trypsin, that is, digestion of proteins, one can study the nitrogen, although I suppose that the effect of pepsin must also be considered. There are certain standard figures that every clinician interested in this field should try to carry in mind. First there is the total fecal fat, which should not exceed 20 per cent of the weight of the dried stool in the normal individual. Then there is the fat loss, which should not exceed from 5 to 7 per cent of the ingested fat. Finally there is the fat split, which should be about 60 to 75 per cent of the total fecal fat. To use these basic figures intelligently, it is desirable that the fat content of the diet be accurately established. Any diet the fat content of which is known can be used, or else one may employ the standard Schmidt intestinal test diet. When milk is given with this diet, the quantity of fat is about 142 Gm. daily; when cocoa is used instead of milk the daily intake of fat is about 112 Gm. A good plan is to administer this weighed diet for three or four days and to collect and analyze the stools of the last two days for their fat values.

DR. HEINRICH NECHELES, Chicago: I should like to say a few words of caution about secretin. The preparation available for intravenous injection in man deteriorates and becomes toxic on standing, as we found in assays carried out over a period of time; it is rather expensive besides. I assume that the previous speakers employed secretin Astra, the Swedish preparation. Furthermore, I believe that the secretin test cannot be interpreted easily. Secretin produces a water secretion of the pancreas containing largely bicarbonates. It seems that the increase in ferments reported by various workers is due primarily to a washing out effect and not to true secretion. It would seem better, therefore, to combine secretin with physostigmine or prostigmine as we have done, or with mecholyl, as has been reported just now. I believe even that secretin is not necessary because we get a response with mecholyl alone. I believe, however, that 15 mg. of mecholyl is a very large dose even for a normal, healthy adult, as we have experienced a number of times. Trypsin seems to be the only ferment in the small intestine that can be identified as of strictly pancreatic origin, and as long as so little is known about duodenal and upper jejunal secretions it is dangerous to conclude from a diminution of lipase and amylase that this is necessarily due to deficiency of pancreatic secretion. It might well be that a slight duodenitis will increase the output of lipase and amylase by the duodenal mucosa. Also when one collects duodenal juice following secretin one must express pancreatic secretion not by the concentration but by the total amount of enzymes. Pancreatic secretion ought to be collected quantitatively and this is extremely difficult, even with a Miller-Abbott tube. The considerable increase in the volume of psychic gastric secretion of old people surprised us. In a recent paper Bloomfield reported that he found no relation of psychic secretion to age. I recalculated his values and found that the volume increase for psychic secretion was 9 cc. for

young and 23 cc. for old persons. This confirms our results. It seems thus that in old persons the vagal secretory gastric mechanism is unimpaired and may even be more responsive than in young persons.

DR. MANDRED W. COMFORT, Rochester, Minn.: Considerable emphasis has been placed by various discussers this morning on examination of stools as a procedure of choice for studying pancreatic function. I agree that the analysis of stools for undigested and unabsorbed foodstuffs gives excellent data about the completeness of digestion, but I do not believe that the data obtained from the study of stools necessarily disclose the true status of the external secretion of the pancreas, since the small bowel may assume part of the digestive functions of the pancreas. Moreover, from the results of examination of stools for undigested and unabsorbed foodstuffs it is not often possible to distinguish disturbances of digestion secondary to pancreatic disease from those secondary to disease of absorption. Thaysen, a Copenhagen investigator, expressed the belief that the loss of more than from 35 to 40 per cent of ingested fat as neutral fat and the loss of more than 3 Gm. of nitrogen in the stools daily are the only observations from the stools which are of significance in the diagnosis of pancreatic disease. Dr. Necheles has brought up the question of reactions. I have given approximately sixty injections of secretin without a single reaction and Dr. Diamond tells me that he has not had a reaction in about 130 experiments. Acetyl-beta-methylcholine chloride (mecholy) in doses of 15 mg. subcutaneously produces considerable discomfort and marked sweating. Patients have not objected to this reaction when they have been warned of it in advance and know what to expect. The technic of removal of the duodenal contents has been criticized. It is certainly true that possibilities of error are inherent in the method but it is the best technic that has been described so far for removal of the duodenal contents. These various methods of studying the function of the cells of the pancreas which produce the external secretion need much further use before final evaluation of their merit can be made. Ten years ago, histamine was considered by some workers to be a stimulant of gastric secretion that would produce a constant and maximal response. Today we know that histamine has not measured up to the earlier expectations. As time goes on we may find that secretin, acetyl-beta-methylcholine chloride and allied drugs have certain disadvantages; but I am sure also that they will possess considerable merit for use in the study of pancreatic secretion.

DR. JACOB MEYER, Chicago: We have been impressed for a number of years with the importance of physiologic studies such as Dr. Ivy has mentioned in order to interpret and evaluate the clinical symptomatology. Much of what he has suggested has been planned, and some of the work is in progress. We likewise have been impressed with the growing significance of old age not only as a social problem but also as a clinical problem, and gastro-enterologists particularly should be cognizant of the manifold problems which are to come to us for solution in the very near future. Dr. Aaron's observation and criticism in a sense is a fair one, but what he has said holds true for almost any type of secretory test on any individual. We recognize the variations in individuals and we must recognize the various factors which may produce these variations. We are not presenting our results as indicating any specific test. We are primarily interested in presenting what is normal for old persons. I should like to call attention to the fact that while the criticism which he has mentioned applies to the individual, statistical analysis of a group of individuals is probably the best means of determining what is normal.

Disinfection.—Destruction of the infecting organism is a logical step in preventing the spread of disease. Concurrent disinfection is the most important of the disinfection procedures. It simply represents an immediate and proper disposal of all the excretions of the patient. Terminal disinfection is essentially a question of cleanliness and is brought about by soap, water and sunshine. Terminal gaseous disinfection has been abandoned, except for destruction of insects and vermin.—Smillie, Wilson G.: Public Health Administration in the United States, New York, Macmillan Company, 1940.

SULFAPYRIDINE AND ITS SODIUM SALT

IN THE TREATMENT OF MENINGITIS DUE TO THE
PNEUMOCOCCUS AND HAEMOPHILUS
INFLUENZAE

JOSEPHINE B. NEAL, M.D.
EMANUEL APPELBAUM, M.D.
AND
HENRY W. JACKSON, M.D.
NEW YORK

During a period of nearly thirty years we have been studying the effect of various forms of therapy in bacterial meningitis. Before the newer chemicals became available the case fatality in pneumococcic meningitis was 100 per cent in our experience and in meningitis due to *Haemophilus influenzae* more than 95 per cent.

The use of azosulfamide and sulfanilamide moderately improved the prognosis. In a series of fifty-three cases of pneumococcic meningitis treated by one or both of these chemicals (and specific serum when available) there were nine recoveries. In treating meningitis due to *H. influenzae* by means of these chemicals and specific serum the results were much less encouraging. In a series of twenty-nine cases there were only two recoveries.

The excellent results obtained with sulfapyridine in pneumonia due to the pneumococcus led us to try the use of this chemical in pneumococcic meningitis. This report is based on a series of thirty cases. The diagnosis was definitely established in each instance by culturing and typing the organisms from the spinal fluid.

Table 1 shows the distribution of the cases by sex, the wide range in age and the causative types. These items are self evident. The other data will be discussed.

Blood cultures were obtained in twenty cases. Of these, ten were positive with six deaths and ten negative with five deaths. From these small groups it would appear that the presence of bacteremia had no particular bearing on the outcome.

Consideration of the foci of infection is of the utmost importance. A definite focus in the ear or mastoid or both was found in seventeen of these thirty cases. In three others there was a strong suspicion of such a focus. In one of the cases with otitis (13) there was a petrositis. In two instances there was a fractured skull and in one a head injury with a possible fracture. While this series shows no record of definite sinus involvement, yet in view of the condition found at necropsy it seems reasonable to assume that an undiagnosed involvement of sinuses, particularly the sphenoids and ethmoids, must have been present in a number of these cases. It is highly probable also that in not a few of these cases there were multiple foci of infection.

It will be noted that in these thirty cases there were ten recoveries. In three of the fatal cases death occurred within twenty-four hours after treatment was begun.

Sulfapyridine was given orally to all of these patients. The dose varied from 4 to 8 Gm. daily, usually at intervals of four hours. Young children have as a rule an excellent tolerance, so that a daily dose of from 4 to 6 Gm. is quite safe in children more than 3 years of age. Infants may be given from 2 to 4 Gm.

When the patient was unable to retain oral medication the sulfapyridine was occasionally administered by rectum in the form of an emulsion with sodium bicarbonate and acacia. The rectal dose was usually twice the oral dose.

The introduction of sodium sulfapyridine has been a distinct advantage. We have used a 2 per cent solution of this compound intraspinally, usually combined with a specific serum, in fourteen instances. The dose

only mild to moderate changes in the red or white blood counts. There have been instances with evidence of renal damage, hematuria occasionally and in one case anuria associated with azotemia. It is probable that in this instance the kidney tubules were obstructed by concretions of sulfapyridine crystals, although this was not proved as no necropsy was obtained. A case which is not included in this series showed similar symptoms and at necropsy there was extensive blocking of the

TABLE 1.—Cases of *Pneumococcic Meningitis Treated with Sulfapyridine*

Case	Sex	Age, Years	Type	Blood Culture	Primary Focus	Treatment and Comment	Result
1	♂	27	4	Negative	Head injury ?	Serum, sulfapyridine orally, azosulfamide.....	Died
2	♂	3 mos.	5	Positive	Otitis, mastoiditis	Serum by vein, sulfapyridine orally, mastoidectomy.	Died
3	♀	6	4	Positive	Otitis ?	Serum, sulfapyridine orally for 2 mos.; no effect on blood; had also panophthalmitis; apparent recovery for 2 weeks and then relapse	Died
4	♂	28	18	Negative	None found	Serum by vein, sulfapyridine orally, large doses; rash, and anuria, high urea nitrogen and nonprotein nitrogen; albumin and red blood cells in urine	Died
5	♂	8	18	Negative	Otitis, mastoiditis	Mastoidectomy, sulfanilamide and azosulfamide; sulfapyridine orally	Recovered
6	♀	50	1	Otitis, mastoiditis	Mastoidectomy, serum, sulfapyridine; died within 24 hours after treatment was begun	Died
7	♂	11	5	Positive	Otitis, mastoiditis	Mastoidectomy, serum by vein and intraspinally; sulfapyridine; red blood cells and sulfapyridine crystals in urine	Recovered
8	♂	13	5	Positive	Upper respiratory infection	Serum by vein, sulfapyridine.....	Recovered
9	♂	1½	4	Positive	Otitis, brain abscess	Brain abscess drained, serum by vein and intraspinally; sulfapyridine	Recovered
10	♀	26	3	Positive	Otitis, mastoiditis	Mastoidectomy before meningitis; sulfanilamide 11 days, sulfapyridine 1 day	Died
11	♀	39	8	Otitis	Sulfapyridine, serum and sodium sulfapyridine intraspinally; died within 12 hours	Died
12	♀	33	1	Otitis	Sulfapyridine; in seventh month of pregnancy.....	Died
13	♂	48	3	Negative	Otitis, petrositis	Reexploration of petrous bone; serum and sodium sulfapyridine intraspinally; sulfapyridine	Recovered
14	♀	50	3	Negative	Otitis, mastoiditis	Mastoidectomy before meningitis; operation revised later; sulfapyridine, sodium sulfapyridine intraspinally; sinus thrombosis and jugular ligation	Died
15	♀	27	3	Negative	Otitis, mastoiditis	Serum intravenously and intraspinally, with sodium sulfapyridine; sulfapyridine	Died
16	♂	5½ mos.	18	Otitis	Sulfapyridine	Died
17	♂	9	3	Negative	Otitis, mastoiditis	Mastoidectomy; serum and sodium sulfapyridine intraspinally; sulfapyridine	Died
18	♂	14	15	Fractured skull	Sulfapyridine; sodium sulfapyridine intraspinally....	Recovered
19	♂	64	18	Sulfapyridine; sodium sulfapyridine intraspinally; died within 24 hours after treatment	Died
20	♂	58	3	Otitis	Sulfapyridine; sodium sulfapyridine and serum intraspinally; developed pneumonia while under treatment	Died
21	♀	1½	14	Positive	Serum; sulfapyridine; developed brain abscess.....	Died
22	♂	44	1	Negative	Mastoiditis	Mastoidectomy; serum; sulfapyridine.....	Recovered
23	♀	45	19	Positive	Otitis	Serum and sodium sulfapyridine intraspinally; sulfapyridine	Recovered
24	♀	46	Beyond 32	Negative	Sulfapyridine; sodium sulfapyridine intraspinally; prompt improvement; medication stopped; relapsed after 17 days; same treatment resumed	Recovered
25	♀	9	Beyond 32	Azosulfamide 8 days; sulfapyridine.....	Died
26	♂	43	21	Positive	Fractured skull	Serum intravenously; sodium sulfapyridine and serum intraspinally two or three times; sulfapyridine; sodium sulfapyridine intravenously	Died
27	♀	62	7	Otitis, mastoiditis	Mastoidectomy; serum and sodium sulfapyridine intraspinally; sulfapyridine; bronchopneumonia	Died
28	♀	8	4	Serum and sodium sulfapyridine intraspinally; sulfapyridine	Recovered
29	♀	1 yr. 11 mos.	4	Positive	Mastoiditis ?	Serum and sodium sulfapyridine intraspinally; serum intramuscularly; sulfapyridine	Died
30	♀	48	1	Negative	Mastoiditis ?	Serum intravenously; sulfapyridine; sodium sulfapyridine intraspinally	Died

Thirty cases; ten recoveries; three patients died within twenty-four hours after treatment was begun.

has been from 10 to 15 cc. after each spinal drainage. We have felt that the intrathecal use of this drug was beneficial. No untoward reactions have followed the administration in this dilution. More concentrated solutions should not be used, as there may be dangerous reactions.

The intravenous use of this compound is indicated particularly when the patients are unable to retain oral medication. In this series the sodium compound was used intravenously in only one instance. However, it was used in seven cases of meningitis due to *H. influenzae* and in other cases the data of which have not as yet been correlated.

The toxic effects of sulfapyridine are too well known to require detailed comment. We have encountered

pelvis, calices and tubules with the sulfapyridine crystals. In this particular instance the blood sulfapyridine level was low, averaging 2 mg. per hundred cubic centimeters in spite of the ingestion of large doses of the drug. No doubt the patient was acetylating most of the sulfapyridine.

Serum has been used in addition to sulfapyridine intraspinally in most instances and occasionally intravenously. The intraspinal dose was from 10,000 to 20,000 units following each lumbar puncture. The intravenous dose varied from 100,000 to 300,000 units.

The importance of the eradication by surgery of foci of infection cannot be overemphasized. The nature of these foci has already been discussed. In our experience it is much more difficult to localize and to eradicate

foci of infection in pneumococcic than in streptococcic meningitis. It is also our impression that multiple foci are more common in pneumococcic meningitis. We believe the difficulty in completely eradicating foci of infection is a factor in the less favorable case fatality in pneumococcic meningitis.

The discouraging results with sulfanilamide and azosulfamide in the treatment of meningitis due to *H. influenzae* prompted us to change to sulfapyridine and its sodium salt.

to search for possible foci of infection. In three of our patients with recovery a mastoiditis was present and a mastoidectomy was performed. Another patient with clinical mastoiditis was not operated on and died. There were two patients with ethmoiditis that were operated on and recovered. Unfortunately the material removed at operation was not cultured. One fatal case followed an operation on the palate. In one patient who recovered, the meningitis was preceded by injury and infection of the orbit.

TABLE 2.—Cases of *Haemophilus Influenzae* Meningitis Treated with Sulfapyridine

Case	Sex	Age, Years	Blood Culture	Treatment	Result	Comment
1	♀	5	Serum; sulfanilamide; mastoidectomy, dural slit; sulfapyridine	Recovered	Otitis, mastoiditis
2	♀	1½	Positive	Serum, also intramuscularly; sulfanilamide; sulfapyridine	Died	Necropsy: diffuse meningitis; temporal lobe abscess
3	♂	16	Negative	Serum; azosulfamide; later sulfapyridine.....	Recovered	
4	♂	2½	Negative	Sulfapyridine	Recovered	Injury and infection of orbit; relapse
5	♀	2½	Negative	Sulfanilamide; sulfapyridine	Died	Followed operation on palate
6	♀	7	Positive	Serum; sulfanilamide and azosulfamide; sulfapyridine; sodium sulfapyridine intraspinally	Died	Upper respiratory infection
7	♀	2	Negative	Sulfapyridine	Recovered	Prompt recovery; one positive spinal fluid culture
8	♂	51	Negative	Sulfanilamide and azosulfamide; sulfapyridine; serum and sodium sulfapyridine intraspinally	Recovered	
9	♂	9½	Negative	Sulfapyridine; sodium sulfapyridine; serum intraspinally	Died	Began as brain abscess; operation; necropsy, large brain abscess
10	♂	2¼	Positive	Azosulfamide; sulfapyridine; rabbit serum intraspinally	Died	Upper respiratory infection; otitis
11	♀	4	Negative	Mastoidectomy; azosulfamide; sulfapyridine; serum and sodium sulfapyridine intraspinally	Recovered	X-ray examination showed mastoiditis
12	♂	1	Negative	Sulfanilamide, azosulfamide; sulfapyridine and serum intraspinally; serum in vein	Died	Necropsy: diffuse meningitis; block
13	♂	3	Negative	Sulfapyridine; sodium sulfapyridine intraspinally...	Recovered	
14	♂	3	Positive	Sulfapyridine; serum and sodium sulfapyridine intraspinally	Died	Block
15	♀	1¼	Positive	Fothergill's serum plus complement; sodium sulfapyridine intraspinally; sulfapyridine	Died	
16	♂	3	Positive	Sulfanilamide; sulfapyridine; sodium sulfapyridine and serum intraspinally	Recovered	
17	♂	1½	Negative	Sulfapyridine; sodium sulfapyridine and serum intraspinally	Died	
18	♂	3	Negative	Sulfanilamide; sulfapyridine; sodium sulfapyridine in vein; sodium sulfapyridine with and without serum intraspinally	Died	
19	♀	4	Negative	Sulfapyridine; sodium sulfapyridine in vein.....	Recovered	Responded within 3 days
20	♀	2	Positive	Sulfapyridine; sodium sulfapyridine intraspinally and in vein	Died	Diagnosis made 2 weeks after onset
21	♂	3	Sulfapyridine orally; inadequate dose; sodium sulfapyridine intravenously	Died	Double otitis media and clinical mastoiditis; no operation
22	♀	5½	Negative	Sulfapyridine orally; sodium sulfapyridine and serum intraspinally; mastoidectomy	Recovered	Relapse; otitis, mastoiditis
23	♂	1 yr. 1 mo.	Negative	Sulfapyridine orally; sodium sulfapyridine and serum intraspinally	Died	Block
24	♂	4	Negative	Sulfapyridine orally; sodium sulfapyridine intravenously	Recovered	No treatment intraspinally
25	♀	9 mos.	Negative	Sulfapyridine orally; sodium sulfapyridine intravenously and intraspinally; small amount of serum intraspinally	Died	
26	♂	22	Sulfapyridine orally; sodium sulfapyridine and serum intraspinally	Recovered	
27	♀	8	Positive	Sulfapyridine orally; sodium sulfapyridine and serum intraspinally; later sulfamethylthiazole orally	Recovered	Ethmoiditis; operation
28	♂	35	Negative	Sulfapyridine orally; sodium sulfapyridine and serum intraspinally	Recovered	Followed submucous resection and ethmoidectomy
29	♀	8 mos.	Negative	Sulfapyridine orally; sodium sulfapyridine and serum intraspinally	Died	

Twenty-nine cases; fourteen recoveries.

We are reporting a series of twenty-nine cases in all of which the diagnosis was definitely established by culturing the organisms from the spinal fluid.

Table 2 shows an analysis of the data with regard to these cases. It will be noted from this table that this form of meningitis is essentially a disease of early childhood, twenty of the patients being less than 5 years of age.

Blood cultures were obtained in twenty-six instances, eight of which were positive. From this small series of cases it would seem that a positive blood culture is an adverse factor in the prognosis, since all but two of the recoveries were in the group with negative blood cultures.

While this form of meningitis appears to be a primary disease in most instances, it is nevertheless important

In this group of twenty-nine cases there were fourteen recoveries. It may be noted that among the fifteen fatal cases there were two with brain abscess, three with block and one in which the diagnosis was made and treatment started after the illness had existed two weeks.

Sulfapyridine and sodium sulfapyridine were administered in much the same manner as described in the treatment of pneumococcic meningitis. In the majority of the cases a specific serum often combined with sodium sulfapyridine was injected intraspinally. It should be noted, however, that sulfapyridine or sodium sulfapyridine or both were used without serum in five of the cases in which recovery occurred.

An endeavor to find a satisfactory method of treating meningitis due to *H. influenzae* is particularly impor-

tant, since for the past several years there has been a sharp increase in the incidence of this disease. This increased prevalence has been noted not only in New York but also in Boston by Fothergill.

SUMMARY

We have presented a series of thirty cases of pneumococcic meningitis with ten recoveries and twenty-nine cases of meningitis due to *H. influenzae* with fourteen recoveries treated with sulfapyridine, its sodium salt or both. A specific serum was usually employed as well. However, we believe, in view of our previous experience, that the lower case fatality in both forms of meningitis is attributable largely to this form of chemotherapy.

NEW CLINICAL ASPECTS OF THE
ANALGESIC ACTION OF
MORPHINE

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Morphine is considered the best pain relieving drug which the clinician has at his disposal, yet there are elements of tolerance, addiction and gastrointestinal disadvantages to its use. It is common knowledge that the drug often causes undesirable constipation. Further, when morphine is given over long periods of time, tolerance develops, and addiction may be the end result. Treadway¹ reports that of a series of 1,276 morphine addicts 325 attributed their original downfall to medical use of this drug. Other authors give conflicting reports, but it is interesting that Adams² states that in Great Britain all the witnesses called before the Departmental Committee except one considered the medical use of morphine as the immediate exciting cause of addiction in a "considerable proportion of drug habitués." Still another drawback to morphine is the frequent necessity of giving large doses, which more quickly leads to tolerance and addiction.

Much work has been done on producing a chemical which might serve as a substitute for morphine. The most notable is, perhaps, dilaudid hydrochloride (dihydromorphinone hydrochloride). It is recognized that, while dilaudid hydrochloride may have certain advantages over morphine, it does not entirely fulfil the requirements for a perfect substitute. As regards other substitutes, Hayman and Fox³ have reported that pantopon⁴ in comparable doses has no advantages over morphine.

The present report considers the use of prostigmine methylsulfate in combination with morphine in a series of approximately 100 cases.

Prostigmine is the dimethylcarbamic ester of m-oxyphenyltrimethyl ammonium methylsulfate. Pharmacologically it is similar to physostigmine salicylate in that it is a stimulant of the parasympathetics and has the power of inhibiting the cholinesterase. It does have the advantage over physostigmine of showing little, if any,

myotic or untoward cardiac effects and of having greater stimulating action on the small intestine. Recently it has been shown by Schweitzer, Stedman and Wright⁵ that prostigmine methylsulfate is the only therapeutic anticholinesterase drug which has a central depressant effect.

The use of prostigmine methylsulfate in myasthenia gravis is now well accepted. Recently it has been used with apparent success in the treatment of deafness.⁶ Further, its use to treat and prevent postoperative ileus and anuria is well established. The rationale in myasthenia gravis and postoperative use rests on the ability of this drug to protect acetylcholine against being destroyed by cholinesterase. The premise as regards deafness is not, at the moment, perfectly clear.

Since Slaughter and Munsell⁷ recently reported that prostigmine methylsulfate potentiates the action of morphine on pressure-pain in cats, it seemed plausible to try out such a combination on the human being. That prostigmine methylsulfate is a safe drug in itself has been shown by Schwark,⁸ Tietze⁹ and others.

The data on patients was obtained from the Robert B. Green Memorial Hospital at San Antonio, Texas, under the supervision of Dr. Alexander Mileau, and from the Edinburgh County-City Hospital at Edinburgh, Texas, under the direction of Dr. L. M. Southwick.

A critical evaluation was made of the following factors:

1. Study of effects of prostigmine methylsulfate-morphine as to effectiveness on different types of pain.
2. Untoward effects of such a combination of drugs.
3. The use of varying dosage of morphine with prostigmine methylsulfate.
4. Determination as to whether or not the combination of these drugs leads to addiction and whether there are withdrawal symptoms after long usage.
5. The use of prostigmine methylsulfate in treating addiction.

RESULTS OF TREATMENT

The patients in this study roughly fall into six groups: (1) trauma, (2) preoperative sedation, (3) postoperative treatment, (4) coronary occlusion, (5) miscellaneous cases and (6) addiction.

1. *Trauma*.—There were approximately fifty cases in this series. They consisted of trauma due to gunshot wounds, stabbings, fractures (simple and compound) and other types of extensive trauma in which the pain made morphine mandatory. As a rule only 8 mg. of morphine with 1 cc. of a 1:2,000 solution¹⁰ of prostigmine methylsulfate was given subcutaneously. In these patients apparent relief of pain came on in from two to ten minutes. In other accident cases of a similar nature in which only 16 mg. of morphine was administered as much relief from pain was not obtained and the onset of relief was longer, i. e. from six to twenty minutes. These observations were made from the time of the injection to the time the patient expressed real relief from pain and discomfort.

Only one minor, aged 15; received this treatment. He experienced excellent relief and there were no untoward effects.

5. Schweitzer, Alfred; Stedman, E., and Wright, S.: Central Action of Anticholinesterases, *J. Physiol.* **96**: 302 (Aug.) 1939.

6. Davis, Carroll T., and Rommel, John C.: Treatment of Deafness and Contiguous Nervous Disorders with Prostigmine, *Arch. Otolaryng.* **29**: 751 (May) 1939.

7. Slaughter, Donald, and Munsell, Donald W.: Some New Aspects of Morphine Action: Effects on Pain, *J. Pharmacol. & Exper. Therap.* **68**: 104 (Jan.) 1940.

8. Schwark, G.: Our Experience with Prostigmine, *Deutsche med. Wchnschr.* **58**: 412 (March) 1932.

9. Tietze, H.: Regarding the Intravenous Use of Prostigmine, *Deutsche med. Wchnschr.* **60**: 402 (March) 1934.

10. Dose of prostigmine methylsulfate used in each case.

The prostigmine methylsulfate used in this study was furnished by Hoffmann-La Roche, Inc., Nutley, N. J.

1. Treadway, W. L.: Further Observations on the Epidemiology of Narcotic Drug Addiction, *Pub. Health Rep.* **45**: 541 (March 14) 1930.

2. Adams, E. W.: Drug Addiction, New York and London, Oxford University Press, 1937, p. 58.

3. Hayman, J. M., and Fox, Herbert: Comparison of the Analgesic Action of Pantopon and Morphine Sulfate, *J. A. M. A.* **109**: 1813 (Nov. 27) 1937.

4. Pantopon is no longer included in New and Nonofficial Remedies.

2. *Preoperative Sedation.*—There were twenty-five cases in this group. Most of them were gynecologic but five appendectomies were included.

By trial, the administration of 5 mg. of morphine plus prostigmine methylsulfate four hours before surgical operation and repeated one hour before the operation proved unsatisfactory in producing sufficient sedation.

Further trials established the following routine as giving the most adequate preoperative sedation:

1. Phenobarbital 0.2 Gm. the night before operation.
2. Phenobarbital 0.2 Gm. four hours before operation.
3. Morphine 8 mg. plus prostigmine methylsulfate thirty minutes before operation.

This schedule appeared to give as good sedation as substituting 16 mg. of morphine instead of the 8 mg. plus prostigmine methylsulfate. At the time of operation this use of prostigmine methylsulfate did not interfere with any surgical procedure. All appendixes were removed in the gynecologic cases, if present.

3. *Postoperative Relief from Pain.*—All these patients had orders for 8 mg. of morphine plus prostigmine methylsulfate on return from the operating room, to be repeated every three hours for three doses and then "as needed." There were five cases of moderate distention in this series following operation. These were relieved by the insertion of a rectal tube and the administration of 0.5 cc. of a 1:2,000 solution of prostigmine methylsulfate every twenty minutes for two doses and then every two hours for four doses if needed. Only one patient required the use of a Wangenstein suction.

4. *Coronary Occlusion.*—Five patients with conditions diagnosed as coronary occlusion were treated in the emergency room with 8 mg. of morphine plus prostigmine methylsulfate. All received relief within ten minutes. They then were given this combination every three hours "as needed." In none of these cases was it necessary to order additional doses of morphine. Three received this form of treatment until death, i. e. from eight to thirty-six hours. The other two were discharged after a few days of hospitalization on this treatment. Previously such patients had always received 16 mg. of morphine. We felt that the results of the combination were as good as followed the use of larger doses of morphine.

5. *Miscellaneous Cases.*—These included bronchiectasis, delirium tremens, kidney abscesses, nephritic pains and the dressing of painful wounds. They required morphine. A typical case follows: A patient with nephritis suffered extreme lumbar pain which 16 mg. of morphine did not alleviate. The combination of 8 mg. of morphine plus prostigmine methylsulfate gave and maintained comfort.

6. *Addiction.*—Only one case of true addiction is presented. The patient was treated over a period of six weeks. He had urethral calculi with periurethral abscesses.

Six years previously he had gonorrhea, followed in one year by stricture of the urethra. At this time he entered the hospital for a urethrotomy. Soon after this operation, periurethral abscesses and a urethral fistula developed which persisted until the present time. At intervals, urethral calculi complicated the picture. The patient was an ambulance driver who gave no history of any drug habits before the urethrotomy. After operation he was given 10 mg. of morphine for pain relief. It became necessary to increase this dose to 16 mg. of this drug. Shortly the patient became

addicted and took as much as 30 mg. at intervals. Three years of this habit brought his admittance to a government hospital. After the hospital discharged him as cured of the drug habit, his urethral difficulties returned and a physician put him back on morphine for relief of pain. He continued to take 16 mg. of morphine. Six weeks prior to admission to the Robert B. Green Memorial Hospital, with the diagnosis of periurethral abscesses, urethral calculi and urethral fistula, he stated that he was taking 30 mg. of morphine every four hours.

A radical urethroplasty was successfully performed. Postoperatively he was placed on 30 mg. of morphine. Two days later 16 mg. of morphine plus prostigmine methylsulfate apparently satisfied him. Reduction of the dose of morphine to 10 mg. gave excellent results for four days. Further reduction to 8 mg. did not suffice.

During this stage of the treatment he had not been told of the use of prostigmine methylsulfate but did comment that his bowel action had returned to normal. When he was told of this treatment, he cooperated well. The wound had healed after four weeks and the catheter had been withdrawn. Voluntary urination was instituted after two trials. At this time 10 mg. of morphine plus prostigmine methylsulfate was still being given and the patient did very well, complaining only of slight nervousness just before his dose. This procedure continued through the fifth postoperative week.

The sixth week 8 mg. of morphine plus prostigmine methylsulfate was ordered. After the second day of this treatment the patient skipped every other dose without ill effects. He was then discharged to a government hospital for observation.

During the time prostigmine methylsulfate was used with the morphine, no withdrawal symptoms were noted.

COMMENT

This study indicates that one-half the accepted dose of morphine when combined with prostigmine methylsulfate in doses of 0.5 mg. gives as good relief as the larger dose of morphine. There were no side reactions noted. An order for 0.5 mg. of atropine was always written, but it was never needed. No apparent tolerance to morphine when used in this combination becomes evident.

There was one case of ruptured appendicitis complicated by peritonitis in which this combination gave satisfactory results. Saegesser¹¹ has reported the use of prostigmine methylsulfate in a series of approximately thirty cases of peritonitis. He comments on the excellent results and says that the untoward effects in this condition make this drug suitable for use as a prophylactic to lessen the danger of postoperative intestinal atony. In our series of cases there were none which showed ileus or anuria following operation.

In all but two cases the combination of prostigmine methylsulfate and 8 mg. of morphine relieved pain. Twice in this series of 100 cases it was necessary to give 16 mg. of morphine instead of the smaller dose; one was a case of extensive gunshot wounds and one of compound fracture.

While no untoward effects were observed following the use of this combination, it is felt that perhaps shock is a contraindication to the use of prostigmine methylsulfate with morphine.

We feel that combinations of 1 cc. of a 1:2,000 solution of prostigmine methylsulfate plus 8 mg. of

11. Saegesser, M.: Prostigmine "Roche," Schweiz. med. Wchnschr. 63: 366 (April) 1933.

morphine is an efficient pain reliever. Further, it is an excellent preoperative sedative and postoperative analgesic. When used before operation, it definitely minimizes ileus, distention and anuria. Levis and Axelmann¹² believe that without prostigmine methylsulfate from 60 to 75 per cent of patients will suffer from one or the other of these conditions. Used post-operatively, enemas and the use of catheterization are decreased.

The one case of addiction treated with prostigmine methylsulfate lends encouragement to the use of this drug in similar cases.

The results in this study would seem to substantiate the experimental work done on this problem. We believe that they bear out the findings of Slaughter and Munsell⁷ that morphine is a cholinergic drug as regards its action on pain. That it is cholinergic in other respects is evidenced by the reports of Slaughter and Gross¹³ on the dog's intestine, cat's blood pressure and toxicity in rats.

Summary Comparing Analgesic Effects of Morphine Alone and in Combination with Prostigmine Methylsulfate and Phenobarbital

Drug Used	Dose	Time for Onset of Action	Mode of Onset	Duration of Action
1.* Morphine sulfate	16 mg.	6-20 min.	Gradual	60-90 minutes
2.* Morphine sulfate Prostigmine methylsulfate	8 mg. 0.5 mg.	2-10 min.	Increased over 16 mg. of morphine alone	90-120 minutes †
3.† Morphine sulfate Prostigmine methylsulfate	5 mg. 0.5 mg.	6-20 min.	Gradual	30-60 minutes
4.‡ Phenobarbital 4 hrs. before surgery Phenobarbital 1 hr. before surgery Morphine sulfate plus Prostigmine methylsulfate, 30 min. before surgery	0.2 Gm. 0.2 Gm. 8 mg. 0.5 mg.	5-10 min.	Gradual	Satisfactory sedation preceding and during anesthesia; most patients in this report received spinal anesthesia when surgery was performed

* Used for relief of pain.

† In several instances, the duration of action exceeded 120 minutes.

‡ Used for preoperative sedation.

One of us is at present investigating the angle of tolerance and addiction in dogs, and preliminary work indicates that prostigmine methylsulfate lessens the tolerance and decreases the chances of addiction to morphine.

It is hoped that this report will stimulate other clinical research as regards this problem.

SUMMARY

1. Excellent relief from pain in a variety of cases was obtained by using 1 cc. of a 1:2,000 solution of prostigmine methylsulfate with decreased amounts of morphine.

2. There were no untoward effects in this group of patients using such a combination.

3. Prostigmine methylsulfate relieves the tonic constipation caused by morphine, since it has a marked stimulatory effect on intestinal peristalsis.

4. Further large scale use of this combination in the relief of pain and in the treatment of addiction is indicated.

5. This work further substantiates the cholinergic action of morphine with regard to its effects on pain.

12. Levis, W. R., and Axelmann, E. L.: *Modern Method for Prevention of Postoperative Distention*, Am. J. Surg. 32: 308 (May) 1936.

13. Slaughter, Donald, and Gross, E. G.: *Some New Aspects of Morphine Action, Effect on Intestine and Blood Pressure; Toxicity Studies*, J. Pharmacol. & Exper. Therap. 68: 96 (Jan.) 1940.

INFLUENZAL MENINGITIS

REPORT OF TWO CASES WITH RECOVERY; ONE CASE COMPLICATED BY PAROXYSMAL TACHYCARDIA

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In 1933 two cases of influenzal meningitis were presented by one of us (E. L. N.) before the Philadelphia Pediatric Society.¹ One resulted in complete cure; the other showed at autopsy a brain almost entirely devoid of exudate. We believed that death occurred in the second case either because of edema of the brain from serum shock or from pressure changes following cisternal drainage. Both these patients were treated with serum, the first with serum of Dr. Dorothy Wilkes Weiss,² obtained from Parke Davis & Co., the second largely with serum obtained from Dr. Margaret Pittman³ of the Rockefeller Institute.

Two further cases of influenzal meningitis are here presented. We believe that they will be of interest because they were consecutive cases with prompt recovery; further, they presented features of interest, particularly the boy aged 5 years, who had an attack of paroxysmal tachycardia.

REPORT OF CASES

CASE 1.—V. S., a white girl aged 5 years, the daughter of a physician, on the evening of Dec. 29, 1939, felt ill, vomited twice and complained of weird and fantastic dreams. She had a rhinitis. The following afternoon she had projectile vomiting and became semicomatose. Twitchings of the upper extremities were observed; she had a high temperature. Neither her past history or her family history was relevant.

She was admitted to the Mercy Fitzgerald Hospital. She was quite stuporous but moved restlessly in the bed. Muscle twitchings were present in all extremities.

Her eyes were deviated, the pupils equal but dilated and reacting sluggishly to light. The fundi were normal. There was no evidence of intracranial pressure at this time.

The pharynx was definitely injected and hyperemic. The sinuses and mastoids were clear and remained so.

Moderate rigidity of the neck was present. Knee jerks could not be obtained. Kernig's sign was positive and Babinski's sign and ankle clonus were not present.

Her pulse rate was 168 a minute, of poor volume but regular. Her respiratory rate was 44, her temperature 105 F.

The blood count on admission was hemoglobin 9.8 Gm., red blood cells 3,510,000, leukocytes 4,550, neutrophils 80 per cent, lymphocytes 12 per cent and monocytes 8 per cent. A complete list of blood counts is given in table 2.

Blood cultures taken at this time and again on Jan. 13, 1940, were negative.

The first spinal fluid withdrawn was opalescent and contained 3,200 cells per cubic centimeter. Pleomorphic influenza bacilli were present and the culture was positive for *Bacillus influenzae*.

She was immediately given a transfusion of 175 cc. of citrated whole blood followed by intravenous injection of 45 cc. of 5 per cent solution of sodium sulfapyridine. A few minutes later she had a severe convulsion, became cyanotic and had extreme respiratory difficulty. The convulsion stopped after a short time and respiration and color improved.

Owing to lack of space, this article appears here without the tables. They will be included in the authors' reprints.

1. Noone, Ernest: *Influenzal Meningitis and Its Treatment with Serum* (Abstr.), Am. J. Dis. Child. 46: 221-222 (July) 1933.

2. Weiss, Dorothy Wilkes, and Huntington, R. W., Jr.: *J. Pediatr.* 9: 462-466 (Oct.) 1936.

3. Pittman, Margaret J.: *Exper. Med.* 58: 683-706 (Dec.) 1933.

Sulfapyridine was continued by mouth, averaging 4 Gm. a day. (The patient's weight was 38 pounds [17 Kg.]).

The following day she remained comatose; rigidity of the neck was extreme. The left ear drum became red and paracentesis was performed by Dr. Cornelius McCarthy. Smear and culture of the exudate were negative.

Influenzal serum had been obtained from the Mulford Laboratory of Sharp & Dohme and 50 cc. was given by vein with another blood transfusion of 100 cc.

On the following day, January 11, Fothergill's influenza serum was received from the Massachusetts Department of Health and 8 cc. was administered into the spinal canal. This was accompanied by 5 cc. of human complement, thus following the procedure advised by Ward and Fothergill.⁴ Lack of complement in diseases due to gram-negative organisms was pointed out in 1924 by Kolmer⁵ and again in 1932 by Ward and Wright.⁶

The amount of serum and complement administered by spinal route was limited by the amount of thickened spinal fluid we were able to withdraw.

Thereafter, the Sharp & Dohme serum was administered intravenously and the Fothergill serum as well as some Sharp & Dohme serum by way of the spinal canal.

A survey of treatment and the condition of the spinal fluid is given in table 1. Progress of the case is depicted in figure 1.

Nausea and vomiting occasionally interrupted the oral administration of sulfapyridine, on which occasions rectal administration of the sodium salt was employed.

On the third hospital day, Jan. 1, 1940, spinal fluid cultures were negative but bacilli were still observed in the smear, an experience contrary to our observations in cases prior to the use of sulfapyridine.

The child was still stuporous on January 2 but reacted more hopefully the next day.

January 5, no fluid could be obtained on spinal tap. No pressure was registered on the manometer, and the Queckenstedt test was positive. We do not like to resort to cisternal drainage in these cases unless it is imperative. Later in the day a satisfactory flow of fluid was obtained.

January 6, serum reaction appeared, consisting chiefly of wheals and an elevated temperature, and was a continued feature of the case for several weeks.

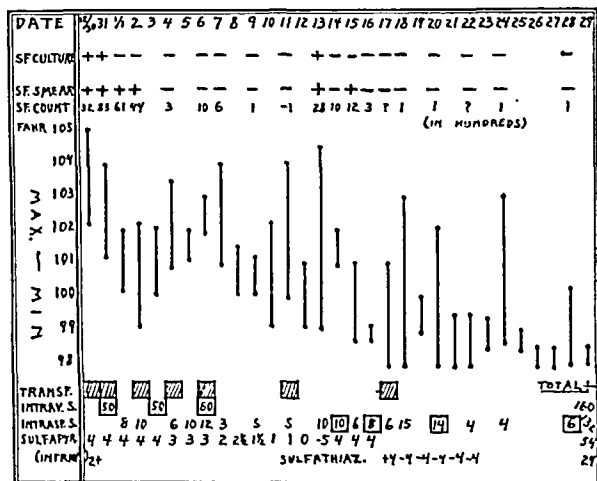


Fig. 1 (Case 1).—Progress and treatment chart. Sharp & Dohme serum designated in blocks. Other serum employed is Fothergill's. S. F., spinal fluid.

The mucous membrane of the lips and mouth and particularly of the gums were now covered with a dirty gray exudate. The gums were spongy. A similar finding was described by Moore

and Forbes,⁷ in a case of pneumococcal meningitis and was attributed by them to the sulfapyridine employed.

Dosage of sulfapyridine was decreased and no serum was given for five days.

Bacilli reappeared in smear and on culture January 13. Sulfapyridine administration was increased and serum was

DATE	3/29	3/30	3/31	4/1	2	3	4	5	6	7	8
S.F. CULTURE	+	+	+	+	-	-	-	-	-	-	-
S.F. SMEAR	+	+	+	+	+	-	-	-	-	-	-
S.F. COUNT	260	300	350	340	19	14	2	-1	-1	-1	-1
in hundreds											
MIN.	105	104	103	102	101	100	99				
MAX.											
INTRAV. S.											
INTRASP. S.											
SULFATHIAZ.											
SULFAPYR.											
Intrav. sod. sulfapyr.											

Fig. 2 (Case 2).—Progress and treatment chart. Sharp & Dohme serum encircled. Other serum employed is Fothergill's. S. F., spinal fluid.

again given. Again culture was negative prior to the disappearance of bacilli from the smear. After January 15 both cultures and smears remained negative. With the exception of moderate serum reactions, the child steadily progressed to a completely normal state.

January 17 sulfathiazole (Squibb) was obtained through Dr. Harrison Flippin and Dr. John Scott, and sulfapyridine was discontinued. Freedom from nausea followed the administration of sulfathiazole.

Later, neurologic examination by Dr. George Wilson showed that the child was completely normal.

CASE 2.—S. H., a white boy aged 5 years, weighing 45 pounds (20 Kg.), recovered more promptly than the first patient and presented the interesting complication of paroxysmal tachycardia.

In earlier years the boy manifested a tendency to hypersensitivity of the mucous membranes and overgrowth of the nasopharyngeal lymphoid tissue. His tonsils and adenoids were removed at the age of 2 years. However, throughout the year of the present infection he had been in excellent health and general physical condition.

March 26, 1940, while sitting on the edge of the bathtub, he fell backward and struck his head heavily in the occipital region on the opposite side of the tub. One may speculate on the influence this accident may have had in opening up pathways of infection and promoting the attack of influenzal meningitis. Certainly there are many cases of meningitis on record immediately preceded by skull fracture.⁸ In this case there was no demonstrable fracture.

The following day he complained of headache. March 28 he returned from school at noon feeling ill, became nauseated and vomited all afternoon. That evening he was irritable and his reflexes were irregular. Kernig's sign was thought to be positive and his pupils were dilated. There was a heavy odor of acetone on his breath.

On the following morning he was admitted to Mercy Fitzgerald Hospital with a provisional diagnosis of head injury. He was intermittently irrational and very restless, his face was flushed and his eyes were rolling. His pupils reacted slowly to light and in accommodation, the left being larger than the right. There was medial strabismus and photophobia. His

4. Ward, H. K., and Fothergill, L. D.: Influenzal Meningitis Treated with Specific Antiserum and Complement, *Am. J. Dis. Child.* 43: 873 (April) 1932.

5. Kolmer, J. A.: *Proc. A. Research Nerv. & Ment. Dis.* 4: 71, 1924.

6. Ward, H. K., and Wright, Joyce: *J. Exper. Med.* 55: 223 (Feb.) 1932.

7. Moore, Mary L., and Forbes, Roy P.: *J. Pediat.* 16: 347 (March) 1940.

8. Prinz, H.: *Chirurg* 5: 544-547 (July 15) 1933.

lips were cherry red. There was no discernible inflammation of the upper respiratory tract or of the ears.

Cervical rigidity was present but intermittent in intensity. He had a bilateral positive Kernig sign. His abdominal reflexes were present, the Babinski sign was not present and the plantar reflex and knee jerks were obtainable.

The temperature was 103 F., the pulse rate 140 and the respiratory rate 32.

X-ray examinations of the skull and cervical vertebrae for fracture or pressure signs were entirely negative.

The white blood cell count was 28,150 cells, 83 per cent neutrophils, 12 per cent lymphocytes and 5 per cent monocytes. Blood chlorides were 476 mg., blood sugar 128 mg., urea nitrogen 10 mg. per hundred cubic centimeters and blood carbon dioxide capacity 32 volumes per cent. A blood culture taken at this time was negative.

On lumbar tap cloudy fluid was obtained under a pressure of 40 mm. of mercury. The cell count was 26,000, polymorphonuclear cells predominating.

The organism observed in the smear was at first thought to be the meningococcus. Accordingly the boy was given 15 cc. of antimeningococcus serum intraspinally and later, when obtained, 20,000 units of Ferry's meningococcus antitoxin in 120 cc. of 5 per cent dextrose solution intravenously. Further amounts of 5 per cent dextrose as well as Hartmann's solution

were of good quality. There was no enlargement of the liver. Cyanosis was present, apparently from the sulfapyridine.

During the night of April 2 an attack of paroxysmal tachycardia began. The rate as registered by the electrocardiograph was 230 a minute. The beats were of good quality early in the day and of poorer quality in the afternoon. The heart was enlarged. The enlargement was confirmed by examination with a portable x-ray apparatus conducted by Dr. J. S. Lehman. There was no suggestion of pericardial effusion. Increased bronchovascular markings in the inner third of the lung fields were compatible with the effect of minimal pressure of active pulmonary hyperemia.

The boy lay quietly in bed as though afraid to move. The vessels of the neck pulsated. There was not much cervical rigidity. The abdomen was flat and there was no enlargement of the liver.

Electrocardiographic studies performed by Dr. Edward Torrance are shown in figures 3, 4 and 5. Tracings were made during the attack, immediately after the attack and eighteen days later. In the opinion of Dr. Torrance, the tracing taken after the attack shows left axis deviation due to dilatation.

Pressure was made over the carotids without effect, but in our opinion the pressure was inefficiently performed and the failure of result inconclusive. The child was given two doses of quinidine, each $1\frac{1}{2}$ grains (0.1 Gm.). The second dose was

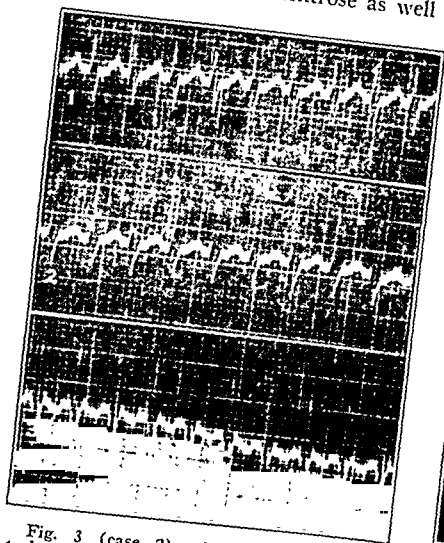


Fig. 3 (case 2).—Auricular paroxysmal tachycardia during attack; cardiac rate 230. It was impossible to distinguish P waves because of rapidity of rate. There was no evidence of cardiac damage.

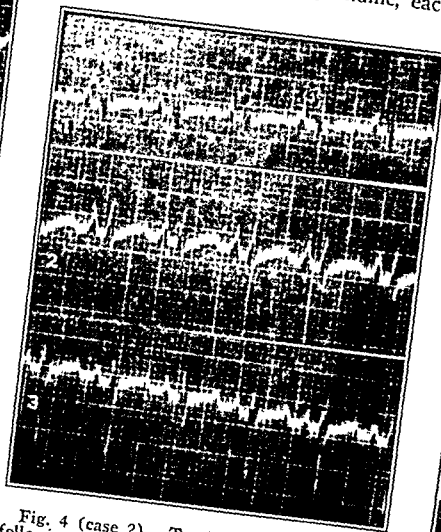


Fig. 4 (case 2).—Tracing taken immediately following attack of auricular paroxysmal tachycardia; cardiac rate 125. Note sharply peaked P waves and left axis deviation, latter probably due to cardiac dilatation during paroxysm.

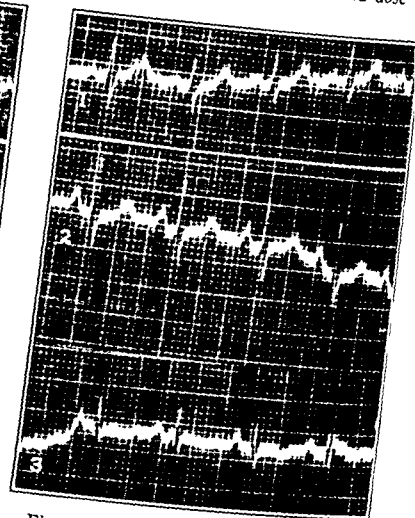


Fig. 5 (case 2).—Normal tracing except for sinus tachycardia. Left axis deviation disappeared. T waves show improvement.

were given into the vein to effect mineral balance. Sulfanilamide 1.5 Gm. was given by mouth on this date, the 29th.

On the following morning, the 30th, the diagnosis of Pfeiffer's bacillus was determined and treatment started with anti-influenzal serum and sulfapyridine. The dosage is summarized in figure 2 and table 3. An initial dose of sodium sulfapyridine was given, 1.5 Gm. in 5 per cent solution, which was followed by a mild reaction consisting of a brief period of respiratory irregularity and muscular tremors.

At this time the child was acutely ill and delirious, his neck was very rigid and his general posture was that of opisthotonos; his knee jerks were no longer obtainable. He picked continuously at the bed clothes and maintained a disconnected discourse in a drawing voice. He exhibited photophobia, and his left pupil was still larger than the right. The spinal fluid was thick and under high pressure, yet on the evening of that day there was a partial block. Manometer pressure was from 0 to 3 mm. of mercury and only 3 cc. could be withdrawn. By morning there was a free flow of fluid.

Since the child had severe reactions when intraspinal serum was used in this case, the serum was given chiefly by vein. The amounts are presented in figure 2 and table 3.

April 1 urticaria was noted, and this continued for ten days after the last administration of serum. The heart appeared to be somewhat enlarged but the beat was regular and the sounds

were given at 4 p. m. The paroxysmal tachycardia stopped abruptly at 5:20. The pulse immediately became stronger and the rate dropped to 125 a minute and continued to lower. Fluoroscopic study by Dr. Lehman showed a definite reduction in the size of the heart as compared with the previous film study.

The boy was rational that day. Pupillary changes were not recorded during the attack, but on the following day the left pupil was smaller than the right, the reverse of the pupillary changes during the earlier and probably initiative stages of the infection. The pupillary changes, drawing speech and tachycardia may have been influenced by inflammatory changes in the vicinity of the fourth ventricle.

The boy now made a rapid recovery. On April 3 the blood sulfapyridine level was 6 mg. per hundred cubic centimeters. From this point treatment was continued with sulfathiazole, secured through Dr. Harrison Flippin. On April 5 the liver was palpable but was no longer palpable by April 7. On the 6th he had a mild cough and his right ear contained a small amount of exudate. Paracentesis was performed by Dr. McCarthy and, as in the first case, culture was sterile. This may have been part of the serum reaction. On the 6th his knee jerks returned. His further progress was steady and uneventful. The majority of the intraspinal and intravenous treatments were performed by Dr. P. J. Devers.

The immune serum employed was *a* supplied by the Massachusetts Department of Health and *b* supplied by the Mulford Laboratories of Sharpe & Dohme. The latter serum is prepared from six strains of *Haemophilus influenzae* of the Pittman type b (smooth),⁹ secured from patients with mixed virulent respiratory and meningal infections.

COMMENT

As six patients with influenzal meningitis¹⁰ were successfully treated in the Philadelphia district during the winter of 1939-1940, there arises the possibility of the prevalence of a strain less virulent than usual. This does not appear to us to be the case. Certainly these two patients appeared as severely ill in the initial stages as other patients observed in previous years. The good results, in our opinion, can be attributed to the more recent available therapy, particularly sulfapyridine and sulfathiazole.

It is essential to make an early diagnosis. This is sometimes difficult, as is illustrated by case 2, owing to involved onset and the early pleomorphic appearance of the organism. Attention was first drawn to the pleomorphic character of influenza bacilli by Slawyk in 1899 and by many other later writers. Once the diagnosis is made, treatment should be vigorously instituted and continued until all danger of reappearance of the organism in the spinal fluid is past. Herein lies one of the chief advantages of chemotherapy, for sulfapyridine and particularly sulfathiazole can be maintained after reactions have made serum treatment embarrassing and even dangerous. However, we believe that we secured beneficial results in the use of serum alone in earlier cases and that the combined treatment with serum and chemotherapy is to the advantage of the patient.

In connection with the early institution of vigorous therapy may be mentioned the tendency of this infection, untreated, to produce heavy exudate with astonishing pressure about the base of the brain, thus accounting for its further tendency for reappearance of bacilli after apparent initial success.

SUMMARY

1. In two consecutive cases of influenzal meningitis 5 year old children were treated with serum (Fothergill and Mulford) and chemotherapy (sulfapyridine and sulfathiazole); recovery occurred in both.

2. Both cases presented interesting features. In the first case a severe shock and convulsion followed intravenous administration of sodium sulfapyridine. A grayish membrane of the lips, gums and mucous membranes of the mouth also developed, presumably due to the sulfapyridine employed. In the second case the infection was immediately preceded by an injury to the head. This case was complicated by an attack of paroxysmal tachycardia.

In both cases an exudate of the middle ear developed during the infection, the culture being sterile in both instances. Blood cultures in both cases were negative.

3. Both sulfapyridine and sulfathiazole are effective in the treatment of influenzal meningitis. There is less tendency to nausea with sulfathiazole.

Wilde Avenue and Cedar Lane.

SPONTANEOUS REDUCTION OF CERVICAL SPINE DISLOCATIONS

J. T. NICHOLSON, M.D.

PHILADELPHIA

Spontaneous reduction of a dislocation of the cervical spine is the restitution of normal relationship between articular facets by permitting active rotations of the head while it functions as the distraction force.

ANATOMY

The aligned position of the cervical vertebrae is controlled by the opposing articular facets. If there is an abnormal distortion or loss of apposition between the articular facets a dislocation of the cervical vertebra prevails. The articular facets of the cervical spine are sliding joints. These are bound by an articular capsule and are supported by the ligaments of the cervical spine.

In the first cervical vertebra the facets are lateral masses which are joined anteriorly by a narrow arc of bone, the arcus anterior, and posteriorly by a similar but longer arc, the arcus posterior.¹ The lateral masses superiorly rest against the occipital condyles of the skull. Below they articulate with the two superior articular facets of the second cervical vertebra. The odontoid has a flattened cartilaginous surface both anteriorly and posteriorly. Across its posterior surface is stretched the transverse ligament from either lateral mass of the first cervical vertebra. From its tip run two alar ligaments and an apical ligament joining the basilar process of the skull. These ligaments are covered with the tectoria membrane, which extends from the basilar process of the occipital bone over the posterior surfaces of the vertebral bodies. The tectoria membrane in turn is covered by the posterior longitudinal ligament, which is also attached to the basilar process of the skull and the posterior surface of the vertebral bodies. Anteriorly the first cervical vertebra is supported by the anterior longitudinal ligament, which extends from the inferior surface of the basilar process of the occiput attaching along the anterior surface of the vertebral bodies. Joining the arcus posterior to the posterior margin of the foramen magnum is the atlanto-occipital membrane. The lower margin of the arcus posterior is joined to the second cervical lamina, and this lamina in turn to the third and it and the successive laminae by ligamenta flava. The inferior facets of the second vertebra are relatively further posterior than the superior and are transitional toward a lateral plane with the articular surface obliquely anterior and caudad. In turn the corresponding superior facets of the third cervical vertebra have a position with the articular surface obliquely posterior and cephalad. Successive articulations of the lower vertebrae in the cervical region are more in the lateral plane but otherwise are similar to those between the second and the third. Interposed between the vertebral bodies excepting the first and second is a fibrocartilage disk. This is covered anteriorly by the continuation of the anterior longitudinal ligaments and posteriorly by the posterior longitudinal ligament.

From the Orthopaedic Clinic of the Children's Hospital.

Read before the Section on Orthopedic Surgery at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

1. Spalteholz, Werner: *Hand Atlas of Human Anatomy*: VI, Philadelphia, J. B. Lippincott Company.

9. Pittman, Margaret: *J. Exper. Med.* 53: 471-492 (April) 1931.

10. Personal communication: Arnat, John, M.D., Episcopal Hospital, one case; Chapple, Charles, M.D., Chestnut Hill Hospital, one case; Harvie, Frederick, M.D., Service of Dr. Joseph Stokes, University Hospital, one case; Wilder, Theodore, M.D., Abington Hospital, one case. Dr. Harvie's case is particularly interesting because the child was only 21 months old. Dr. Chapple's patient was 2½ years of age. Both these children were treated with sulfathiazole.

CLASSIFICATION

The dislocation is common in the upper two cervicals. This may be due to the leverage of the head and the horizontal position of the facets. The dislocation is described as anterior, right or left rotary, posterior

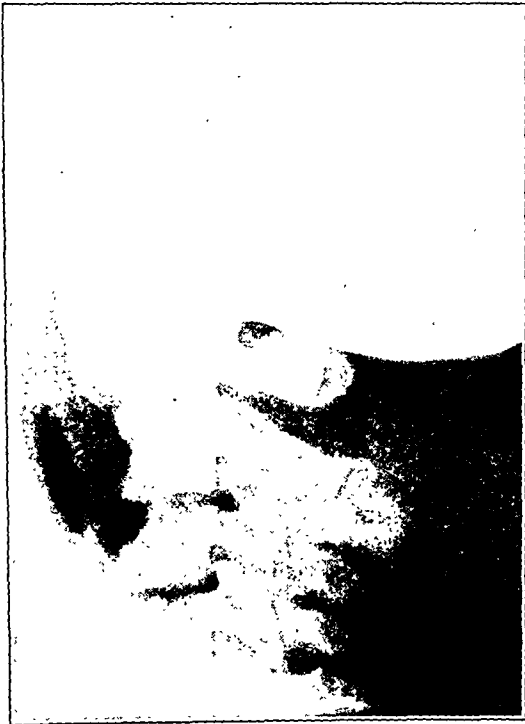


Fig. 1 (case 2).—Side view of the typical position of the head with a right unilateral rotary dislocation of the first cervical vertebra.

and right and left lateral. A fracture of the odontoid or the accessory processes generally accompanies the latter two types. Both articular facets are displaced in all but the rotatory dislocations.

ETIOLOGY

Cervical dislocations may result from trauma, infection, paralysis or congenital defect. Traumatic dislocations are frequently associated with a fractured odontoid or an accessory process. Automobile accidents, falls on stairs, falls from bed, sudden turns of the head, and postoperative overcorrection of torticollis are some of the associated accidents.

Following infection, either in the vertebral bodies or in adjacent cervical tissues, the dislocation is occasionally spontaneous.² The ligaments supporting the cervical vertebrae become relaxed as a result of bone destruction, joint distention or bone decalcification. The vertebrae are destroyed by pyogenic, tuberculous or syphilitic osteomyelitis. The distention of the joints may be from the hyperemia induced by the adjacent infection or from direct extension of infection, such as sinusitis, pharyngitis, tonsillitis, mastoiditis, adenitis and dental abscesses through the neighboring cervical tissues. Decalcification of bone has been reported in the presence of hyperemia resulting from an associated infection.³

2. Jones, R. W.: Spontaneous Hyperemia Dislocation of Atlas, *Proc. Roy. Soc. Med.* 25:586, 1932.

3. Greig, D. M.: Fracture and Dislocations of the Odontoid, in *Clinical Observations on the Surgical Pathology of Bone*, Edinburgh, Oliver & Boyd, 1931. Leriche, R., and Poligard, A.: *The Normal and Pathologic Physiology of Bone*, St. Louis, C. V. Mosby Company, 1928.

Paralytic dislocations from muscle imbalance have occurred in the subacute stage of poliomyelitis.⁴

Congenital absence of the odontoid⁵ and anomalies in the cervical facets are responsible for some cervical dislocations.

DIAGNOSIS

There are definite clinical manifestations which have been described by several authors that lead one to suspect a cervical dislocation. The head is held in a torticollis position. In unilateral dislocations the head is tilted to the side of the dislocation and the chin rotated away from it. The head can be flexed only a few degrees to the opposite side and the chin cannot be rotated as far to the dislocated side. The head is in flexion and extension accentuates pain. The patient frequently supports his head with his hands when rising from a prone position. The entire body is turned when the subject attempts to see over the opposite shoulder. Pain is referred to the occiput and mastoid in dislocations of the upper cervicals. These areas are sometimes tender to touch. The mouth may be difficult to open because of the flexed position of the head. If the pharynx can be seen it will be noticed to bulge to the side opposite the dislocation, if it is unilateral. The paraspinal muscles are prominent posteriorly on the side opposite the dislocation. Occasionally a sensation of grating is experienced with attempted rotation of the head. Dysphagia and voice change seldom occur.

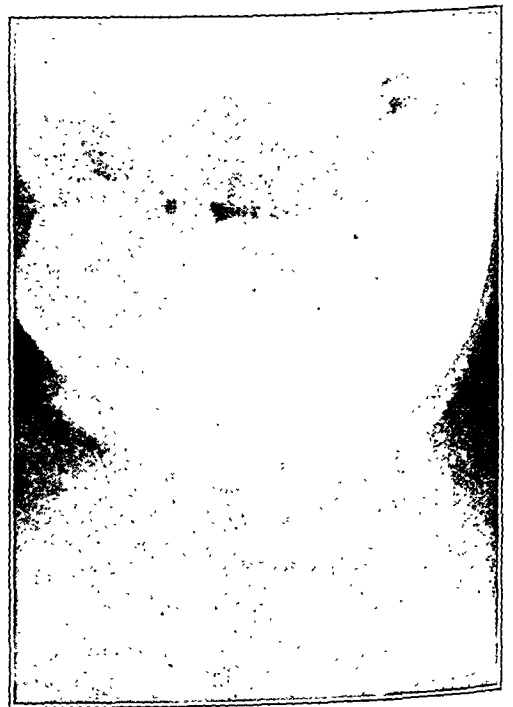


Fig. 2 (case 2).—Front view of the typical position of the head with a right unilateral rotary dislocation of the first cervical vertebra.

Paralysis is rare in the subject who survives the initial dislocation force. If there is paralysis, it is evidenced mainly in the arms.

The x-ray film verifies the diagnosis (figs. 1, 2, 3 and 4). In dislocations of the first cervical vertebra the

4. Coutts, M. D.: Atlanto-Epistropheal Subluxation, *Arch. Surg.* 29:297 (Aug.) 1934.

5. Roberts, S. M.: Congenital Absence of the Odontoid Process Resulting in Dislocation of the Atlas, *J. Bone & Joint Surg.* 12:923 (Oct.) 1933.

lateral view reveals a lordosis of the cervical spine with the anterior arch of the first cervical extending anterior to the odontoid, unless the odontoid is fractured. In the other cervical dislocations the body of the dislocated vertebra projects beyond the anterior border of the vertebra. The posterior arch of the dislocated vertebra appears broader because it is tilted. The posterior borders of the vertebral bodies do not form a continuous arc but angle at the site of the dislocation.

The anteroposterior view discloses the spine of the dislocated vertebra pointing to the opposite side from which the chin is rotated. The spinous processes of successive vertebrae gradually appear toward the midline.⁶ Visible between the first and second vertebrae is the greater width of one articular space. In the other cervical vertebrae there is an increased distance between the transverse processes on the one side and a decreased distance on the opposite side. In a forward displacement of the first cervical both articular spaces are decreased. In forward displacement of the other vertebrae there is a diminished distance between the transverse processes, and the intervertebral space is narrowed or obliterated. In lateral displacements the odontoid appears nearer one lateral mass than the other, and in the succeeding vertebra the transverse process and vertebral body project farther to one side.

METHOD OF REDUCTION

The spontaneous method is developed from Stookey's⁶ treatment of injuries of the cervical spine in which hyperextension of the neck was obtained by compressing the upper edge of an air mattress with adhesive tape. The technic varies in spontaneous reduction in that the subject is placed recumbent with his shoulders at the upper margin of three short mattresses tiered on a fracture bed (fig. 5). The head is not supported; its weight distracts the joints of the cervical spine and holds the neck in hyperextension. No apparatus, such as a Sayre collar or skeletal traction tongues, is used. The head of the bed is elevated on shock blocks to prevent the subject from sliding. Buck's extension is employed on both legs of small children in addition to elevating the head of the bed. The position at first may be uncomfortable from strain on the anterior musculature of the neck, in which case the subject is shifted toward the foot of the bed so that the neck rests over the end of the mattress, thus receiving some support. Gradually in the following twenty-four to forty-eight hours the subject is positioned toward the upper end of the bed until the neck is beyond the mattress and the head is hanging free.

After an additional twenty-four to seventy-two hours with the head hanging free, the dislocation is found to be reduced. This is determined by the ability to rotate passively and flex laterally the cervical spine an equal distance to either side.

X-ray examination is facilitated by lifting the mattress with the subject onto a stretcher. This does not disturb the position of the head. The films are taken in the anteroposterior and lateral position without moving the head by holding the cassette on the side or in back of the neck.

Reduction is maintained by a plaster bandage from head to pelvis. It is necessary to have the chin and

forehead included to prevent flexion of the head, which would cause redislocation. The cast is extended to the pelvis to guard the spine against flexion and to distribute its weight on the iliac crests. The method of applying the plaster cast is an adaptation of that advocated by Brookes⁷ in 1933: The subject is transferred from the mattress without supporting the head to the canvas sling of an Abbott frame so that the back rests on the sling and the head hangs dependent over the end. In this position the body jacket is applied. When this dries sufficiently to withstand pressure, a table of equal height as the sling is pushed beneath the subject. The sling is released, which permits the table to support the subject's trunk. The frame and sling of canvas are removed. A 4 inch muslin bandage with a longitudinal

Cervical Dislocations with Spontaneous Reduction

Case	Sub- ject	Age, Years	Etiology	Site	Complication	Result
1	D. S.	3	Spon- taneous	1st anterior	3 recur- rences	Reduction; surgical fixation
2	W. S.	10	Spon- taneous	1st right rotary	None	Reduced
3	B. T.	8	Spon- taneous	Occiput right lateral, 1st left rotary	None	Reduced
4	C. R.	6	Spon- taneous	2d right rotary	None	Reduced
5	R. J.	11	Spon- taneous	2d right rotary	None	Reduced
6	M. D.	3½	Trauma	1st anterior	Fracture odontoid	Reduced
7	D. P.	5	Trauma	2d rotary	Ear infection	Unreduced
8	J. B.	7½	Trauma	2d rotary	None	Reduced
9	M. P.	4	Trauma	2d rotary	Respiratory infection	Unreduced; surgical fixation
10	J. D.	60	Trauma	1st anterior	Fracture odontoid	Reduction; delirium tremens and pneumonia; death
11	J. W.	25	Trauma	5th rotary	Fracture of 6th cervical; weakness of arm muscula- ture	Reduction of dislocation; fracture unreduced

slit in its midportion, permitting it to be slipped over the patient's head, to run beneath the chin and occiput, is arranged so that the ends may be tied behind the operator's back.⁷ In this way the operator can exert traction and control the amount of extension of the neck. The extension that occurs at the occipital-axial joint is not necessary and not desirable, as it will fix the subject's head looking heavenward and make feeding and balance difficult. The head cast is then applied over the traction bandage, which can be withdrawn after the head and body parts of the plaster cast are joined. The subject is allowed to sit up the day after the application of the plaster cast. He is permitted to walk the third day and is discharged as soon as he can navigate without difficulty.

The dislocations are held from twelve to sixteen weeks in plaster and eight additional weeks in a Thomas collar. The Thomas collar is necessary to permit rehabilitation of the cervical muscles. These muscles have undergone marked atrophy. In this condition they fatigue readily. Strain is then thrown on the ligamentous structures of the cervical spine. This strain

6. Stookey, Byron: Treatment of Fractures: The Management of Fracture Dislocations of the Vertebrae Associated with Spinal Cord Injuries, *Am. J. Surg.* 26: 513 (Dec.) 1934.

7. Brookes, Theodore: Dislocations of the Cervical Spine, *Surg., Gynec. & Obst.* 57: 772 (Oct.) 1933.

CASE 7.—D. P., a boy aged 5 years, fell from bed Aug. 4, 1938. The complaint was pain on the left side of the neck and inability to move the head. X-ray examination revealed a dislocation of the second cervical vertebra. After one week the dislocation failed to reduce with dependent head traction. (Great difficulty was encountered in keeping the patient in a satisfactory position. A discharging ear also developed.) Manipulation of the neck by Taylor traction and Walton maneuver was unsuccessful. A body jacket was applied and worn for three months. Six months after the cast was removed there was no change in the position of the vertebra. The subject subsequently moved to California.

CASE 8.—J. B., a boy aged $7\frac{1}{2}$ years, had a series of infections of the upper respiratory tract during the winter and had just finished convalescing from an acute pharyngitis. On March 14, 1939, he was permitted to return to school and was riding in the rear seat of a sedan when it was struck by another car. The child was thrown to the floor of the sedan and sustained a bump on the head. Examination at a local hospital was negative for injury. The child played with other children that afternoon. The following morning he awakened with a stiff neck. The head was tilted to the right and the chin rotated to the left. There was pain on attempted motion of the neck. Physical examination was negative except for pain and the characteristic position of the head. The x-ray appearance was

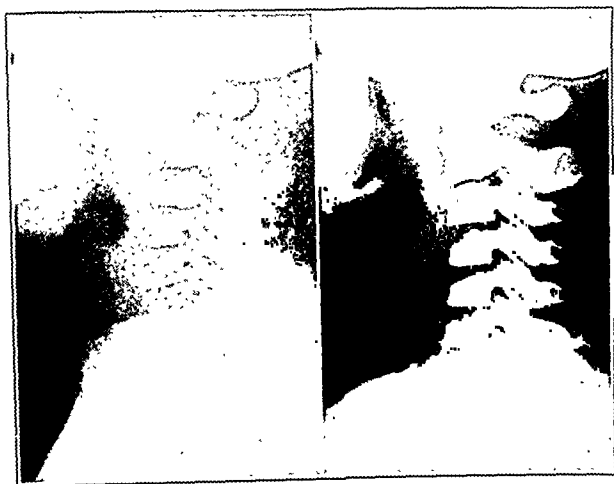


Fig. 7 (case 6).—(a) A fracture through the base of the odontoid with anterior dislocation of the first cervical reduced spontaneously and (b) united after three months of immobilization in plaster.

interpreted as a rotary displacement of the right inferior facet of the second cervical vertebra on the third. The child was hospitalized and after forty-eight hours of dependent head traction the dislocation was clinically and roentgenologically reduced. A plaster cast was applied and worn until May 12. A Thomas collar was worn for an additional month. On March 15, 1940, x-ray examination showed a normal position of the vertebrae and clinical examination was negative.

CASE 9.—M. P., aged 4 years, a feeble-minded boy, fell from his crib eight days after a cleft palate operation. A dislocation of the inferior right facet of the second cervical vertebra was diagnosed by x-ray examination, Dec. 23, 1939. This dislocation failed to reduce spontaneously. An infection of the upper respiratory tract and sinusitis developed. The dislocation could not be reduced by manipulation. An open operation was done March 26, 1940, but reduction could not be obtained. Further deformity was averted by wiring the second and third cervical laminae together. June 5 the position had been maintained two weeks after plaster fixation had been removed.

CASE 10.—J. D., a man aged 60, had delirium tremens, fell down stairs May 30, 1935, sustained a fracture of the odontoid with anterior displacement of the first cervical vertebra and a fracture of the right humerus. He was admitted the same day to the Philadelphia General Hospital. There was no neurologic involvement. It was necessary to feed him through a

nasal tube because of impending delirium tremens. After four days a decubitus ulcer developed on his chin from the Sayre collar traction. Dependent weight of the head was then tried. In twenty-four hours reduction had been spontaneously accomplished. A cast was applied from the head to the pelvis. He tore this cast off twenty-four hours later and was then transferred to the psychiatric ward. The dislocation recurred but no symptoms indicative of cord pressure developed up to the time of his death from pneumonia six weeks after admission.

CASE 11.—J. W., a man aged 25, on Aug. 10, 1937, dove into the breakers at the beach. He was helped from the water. His hands pained and lost their grip and he could not elevate his arms. His legs gave him no support. He was admitted to a local hospital and Sayre traction was applied. An ulcer developed on his chin after seven days.

On September 4 he was transferred to the Philadelphia Orthopaedic Hospital. He had no power in the left hand and marked weakness of the right hand, shoulders and upper arms but no sensory disturbance. The lower extremities were normal except for hyperactive reflexes.

X-ray examination revealed a forward position of the fifth cervical vertebra on the sixth with a compression fracture of the latter.

Since muscle power had steadily improved, the head was placed in a dependent position September 11. X-ray examination revealed excellent alignment five days later. There was, however, extensive edema of the scalp. A jacket was applied September 16 and the subject was ambulatory September 19. A few days later it was necessary to change the cast, as it had become loosened about the head when the edema subsided.

The reduction of the vertebral fracture was not obtained in this case, as the position of hyperextension was not maintained. The patient regained complete power in his arms, had no symptoms referable to his neck, and returned to work in four months as an electrician.

SUMMARY

A spontaneous method of reducing dislocation of the cervical spine proved applicable and successful when other methods could not be applied or had to be discontinued because of lack of the patient's cooperation. Presence of infection or appearance of a decubitus ulcer on the chin. This method of reducing uncomplicated dislocation of the cervical spine was tried on nine children and two adults. The method was uniformly successful in the reduction of spontaneous dislocation. It failed in two traumatic dislocations of the second cervical vertebra. The dependent head theoretically was not applicable in all cases immediately after a traumatic injury. It should not be used in posterior dislocations. Edema of the scalp was a complication arising from the dependent position of the head of one adult. In the two failures there was a danger of spreading a respiratory infection through the sinuses or the middle ear. The reduction was determined clinically by symmetrical rotation and lateral flexion on passive motion of the head. X-ray examination was made without disturbance to the position of the head.

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ABSTRACT OF DISCUSSION

DR. W. H. VON LACKUM, New York: Dr. Nicholson has presented an interesting review of cases of the spontaneous and traumatic dislocations of lesser degree, treated by a method not previously described. In recent years much interest has been shown in lesions of the cervical spine which present this clinical picture of a painful neck, tilted to one side and rotated to the opposite side and associated with muscle spasm. They are the lesions of the atlanto-epistropheal and of the lower cervical spine, associated with trauma exudation or inflammation and an occasional case of paralysis and congenital anomaly in or about the atlanto-epistropheal and lower joints of the

cervical spine. In the atlanto-epistropheal region they are, according to Coutts, rotation deformities, distention-subluxations, dislocations and fracture dislocations. That a fine line of distinction between the rotation deformities, subluxations and slight dislocations has not been made until recently is evidenced by the lack of uniformity in the various older descriptions of the pathology. However, in the exudative reactions in and about the atlanto-epistropheal joints there does exist this unstabilizing pathologic process in joints otherwise stable, which is an entity in itself and one that is as well recognized as the traumatic dislocations and fractures encountered in the lower cervical region. The unstable nature of these joints under conditions of mild stresses and trauma indicated by their capacity to subluxate and dislocate further typifies the mechanical setup in the spinal mechanism where ranges of mobility are great. In my experience at the New York Orthopedic and other hospitals I have found that in gentle head halter traction, at times assisted by manipulation, later supported by head helmet body jackets and removable collars, we have a fairly dependable and satisfactory form of treatment. This of course admits the tendency of these lesions to recur and the occasional failures that necessitate surgical fixation. Dr. Nicholson is offering an additional form of therapy which, if we choose, we may use safely in these cases and apparently a form of treatment that will succeed in some of the cases in which the other more recognized forms of treatment fail. While his series is small, his high percentage of successful reductions and their subsequent stability, as shown by adequate follow-up, speaks well for the method. He has noted some contraindications. Positive indications would seem to hinge around cases with lesions associated with chin decubitus, with mandible injury, painful cervical adenitis and parotitis, as well as among those cases that fail with traction and manipulation.

DR. BARBARA B. STIMSON, New York: Dr. Nicholson's paper has been most enjoyable. He has not been fair, however, to his own ingenuity to call his method a "spontaneous" reduction! Actually, the method is that of traction with the weight of the head exerting the pulling force on the cervical vertebrae by virtue of the described position. The spontaneity has been considerably assisted by the doctor. The series of cases has interested me greatly. I have not had the opportunity to study so many of the complete dislocations, and those I have seen, six in all, were all of traumatic origin. Of these two without fracture were reduced by manipulation. The others were all associated with fracture. One was reduced by traction on an air mattress, as described by Dr. Stookey, one by direct head traction, one was operated on and one refused operation, though reduction could not be maintained. He subsequently went on to spontaneous fusion in a partially corrected position. Over 250 cases of incomplete dislocation have been treated by head traction in the majority of instances. There are two questions I should like to ask. Dr. Nicholson says that his method is not applicable to early traumatic cases. How does he treat them? I feel strongly that the earliest possible reduction of dislocations and fractures is not only easiest but also does least damage to the adjacent soft parts. Surely he would not keep his patient on ice, as it were, until he felt it was safe to apply his method. I have been much troubled by nausea and vomiting in patients treated by traction, either by the Stookey method or by direct head pull. I would think that the extreme position described by Dr. Nicholson would tend to increase this discomfort, and I would like to ask him if this is so.

DR. JESSE T. NICHOLSON, Philadelphia: Dr. Stimson's inquiry as to why measures are not taken to reduce the dislocation at once should be qualified. It is not customary in Philadelphia any more than in New York to neglect the early treatment of the subjects. The delay is suggested before placing the head dependent, as this position might add to the local cord edema in the acute case. It therefore should not be tried until this complication is minimized. But two adults are included in the series. Both have developed pressure sores on the chin following several days traction with a Sayre collar.

Nausea was a minor complaint in one adult. This subject, however, developed extensive edema of the scalp after the head hung three days. When the patient became ambulatory in a plaster cast, the edema subsided so that in four days it was necessary to apply another cast for adequate fixation of the head.

Clinical Notes, Suggestions and New Instruments

SULFATHIAZOLE URINARY CALCULI IN THE KIDNEYS, URETERS AND BLADDER

IN THE ABSENCE OF MARKED URINARY CHANGES FOLLOWING SULFATHIAZOLE THERAPY

SAMUEL A. LOEWENBERG, M.D., NORMAN G. SLOANE, M.D.,
AND PAUL CHODOFF, M.D., PHILADELPHIA

Sulfathiazole (2 sulfanilamide-thiazole) is the newest of the group of chemotherapeutic agents employed in the treatment of pneumococcal pneumonia. Its efficacy in pneumonia is being thoroughly investigated in many of the larger hospitals in this country. Clinical reports¹ and our own results show that in its therapeutic effects sulfathiazole in pneumonia compares favorably with sulfapyridine and that it is preferable to sulfanilamide. It also has the added advantage of being less toxic and less likely to cause some of the complications encountered after the use of either of these other drugs. Since sulfathiazole is still on trial it is important to record any of the complications or sequelae that may arise from its use. Reinhold, Flippin and Schwartz² observed that sulfathiazole is not as readily reabsorbed from the kidney tubules as are sulfapyridine and sulfanilamide. Gross, Cooper and Scott³ reported the formation of sulfathiazole crystals in the distal collecting tubules of rats' kidneys after the administration of sulfathiazole. Pepper and Horack⁴ reported the first instance of crystalline sulfathiazole concretions in the renal tubules of a patient treated for pneumonia with sulfathiazole. Our case is, to our knowledge, the second proved case of sulfathiazole renal concretions and the first in which there were no clinical signs of kidney inefficiency. Added interest in the case was the development of acute vegetative endocarditis and hepatic and splenic necrosis, which may be explained on the basis of the pneumococcemia and is not attributed to any toxic effect of the drug.

REPORT OF CASE

History.—H. S., a woman aged 49, was admitted to our service at the Philadelphia General Hospital March 29, 1940, with signs of left basal pneumonia.

She became ill March 17 with what was considered a cold or grip; her symptoms became progressively worse and she was sent to the hospital twelve days after the onset of her illness. On admission she complained of chills, pain in the chest, dyspnea, cough and hoarseness; there was blood-streaked expectoration.

Examination.—The patient was stout; she was thoroughly conscious and alert. The temperature was 102 F., the pulse rate 120 per minute and the respiratory rate 30 per minute. Her face was flushed; she had herpes labialis; the veins in her neck were distended and she was dyspneic.

The heart was enlarged and fibrillating, the heart rate being 160 per minute, and there was a suspicion of a murmur at

From the Medical Service of the Philadelphia General Hospital and the Jefferson Medical College of Philadelphia.

1. Flippin, F. H.; Schwartz, Leon, and Rose, S. B.: The Comparative Effectiveness and Toxicity of Sulfathiazole and Sulfapyridine in Pneumococcal Pneumonia, *Ann. Int. Med.* 13: 2038 (May) 1940. Thornton, W. B.; Brown, W. H., and Wilson, J. S.: Clinical Toxicity of Sulfanilamide and Sulfapyridine, *J. A. M. A.* 114: 1605 (April) 1940.

2. Reinhold, J. G.; Flippin, H. F., and Schwartz, Leon: Observations on the Pharmacology and Toxicology of Sulfathiazole in Man, *Am. J. M. Sc.* 109: 393 (March) 1940.

3. Gross, P.; Cooper, F. B., and Scott, R. E.: *Urol. & Cutan. Rev.* 44: 205, 1940.

4. Pepper, D. S., and Horack, H. M.: Crystalline Concretions in Renal Tubules Following Sulfathiazole Therapy, *Am. J. M. Sc.* 100: 674 (May) 1940.

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the mitral area which could not be timed because of the fibrillations. The blood pressure was 120 systolic, 80 diastolic.

The lungs showed evidence of lobar consolidation at the left base.

The abdomen was distended; the liver extended 11 cm. below the right costal margin; it was soft and its edge was rounded; the spleen was readily palpable. There was no ascites or superficial edema.

Sputum typed immediately after admission showed pneumococcus type XXV. The blood culture was positive within twenty-four hours for pneumococcus type XXV. Analysis of the blood showed hemoglobin content 68 per cent, erythrocytes 3,100,000, leukocytes 19,200, polymorphonuclears 80 per cent, lymphocytes 18 per cent, monocytes 2 per cent. The Wassermann and Kahn reactions of the blood were plus 4.

The first specimen of urine gave an acid reaction; specific gravity was 1.020; tests for albumin and sugar were negative; there were no casts; an occasional leukocyte was present.

Course in the Hospital.—Soon after admission, in addition to digitalis, she was given 3 Gm. each of sulfathiazole and sodium citrate, which dose was repeated in four hours; subsequently she received 1 Gm. each of sulfathiazole and sodium citrate every four hours until 25 Gm. had been given. April 1, the end of the fourth day, her temperature reached normal by lysis and she showed general improvement; at this time the administration of sulfathiazole was discontinued.

April 3 she had a relapse; the temperature rose to 103 F., the respiratory rate to 45 and the pulse rate to 120. She was extremely hoarse; the heart rate was regular and there was a loud systolic murmur audible over the entire precordium. The blood pressure was 130 systolic, 50 diastolic. The lungs showed an extension of the consolidation to a somewhat higher level on the same side. A profuse diarrhea developed and she became jaundiced. A second blood culture was positive for pneumococcus type XXV. Sulfathiazole and sodium citrate 1 Gm. each was ordered to be given every four hours, and she was placed in an oxygen tent. Her mind was clear.

April 6 she felt better; the temperature was 100 F. T. Lungs showed signs of resolution. The heart showed good compensation; the pulse rate was 100; there was a loud harsh systolic murmur over the body of the heart.

April 7 the temperature was 105.4 F., the pulse rate 152 and the respiratory rate 60. Her mentality was clear. There was

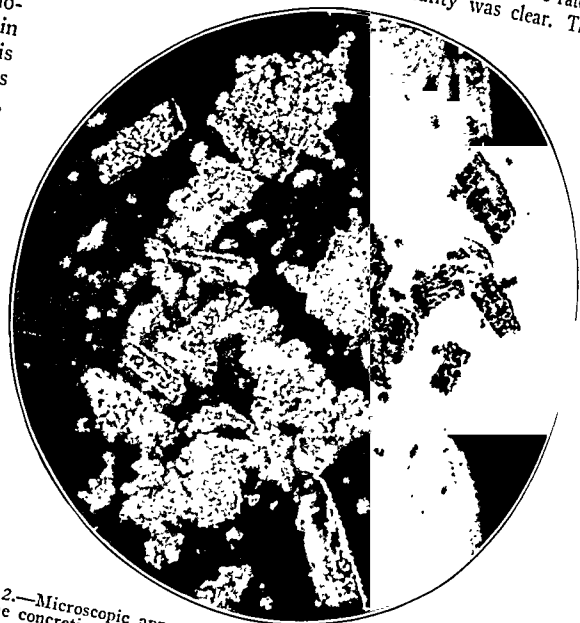


Fig. 2.—Microscopic appearance of crystals of acetylsulfathiazole taken from the concretions.

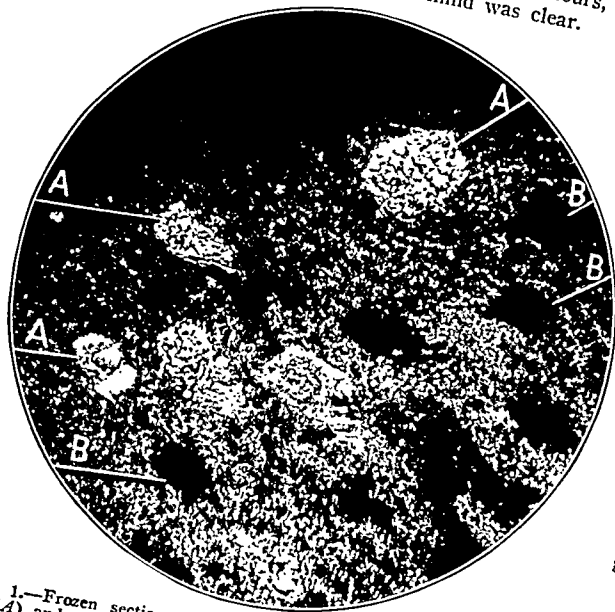


Fig. 1.—Frozen section of kidney showing acetylsulfathiazole concretions (A) and collecting tubules (B).

April 5, because of the pneumococcemia and endocarditis, a tentative diagnosis of acute bacterial endocarditis was suggested and the administration of 100,000 units of type XXV pneumococcus serum was attempted. Though she had not shown any serum sensitivity to the usual tests, a severe chill developed and the temperature rose to 105.4 F. (axillary) after only half of the 100,000 units had entered her vein. Further administration had to be discontinued.

tubular breathing near the angle of the right scapula; the liver and spleen were very large; the patient, notwithstanding the dyspnea, seemed fairly comfortable.

April 8 there was no change in her general appearance or in her clinical manifestations. The heart rate was rapid and regular; sounds were muffled and the murmur was not audible. At 3 p. m. she suddenly died.

During the patient's entire stay in the hospital (ten days she received, in addition to symptomatic treatment, 52 Gm. of sulfathiazole. Though the temperature reached normal on the fourth day, she had a relapse and remained acutely ill, distressingly dyspneic and quite cyanotic; these symptoms were not relieved in the oxygen tent or by other measures. The heart rate slowed and the rhythm became more regular under the influence of digitalis, but a loud systolic murmur developed over the body of the heart which was audible with equal intensity over the entire precordium. The blood pressure remained fairly constant between 126 systolic, 70 diastolic, to 130 systolic, 60 diastolic, and the day she died it was 130 systolic, 50 diastolic. She was mentally alert until the last. At no time did she complain of urinary symptoms. Twenty-four hours before death the temperature rose to 105.4 F.; the heart murmurs disappeared and there was evidence of cardiac dilatation. Death was sudden.

The blood counts made during her stay in the hospital are given in table 1.

The blood Wassermann and Kahn tests gave a plus 4 reaction. Blood urea was 19 mg. per hundred cubic centimeters on admission and 20 mg. several days later. Blood cholesterol was 118 mg. with 10 per cent esters. Blood sulfathiazole levels were from 5 to 7.6 mg. per hundred cubic centimeters. Results of urinalyses are given in table 2.

Culture of the urine on April 3 gave negative results. The fluid intake and output were within normal proportion. Culture of the feces on two occasions showed an unusual predominance of *Staphylococcus aureus*.

Autopsy was done by Dr. H. G. Schlumberger.

External Examination.—The body showed no cyanosis or edema. The skin had a slightly icteric tint but otherwise no abnormal pigmentation was noted.

Internal Examination.—Both pleural spaces were almost obliterated by dense fibrous bands; no free fluid was present. The peritoneal surfaces were smooth and glistening; the mesentery and omentum contained a great deal of fat. No free fluid was present in the peritoneal cavity, and the normal visceral relationships were preserved.

Pericardium: The surfaces were thin, smooth and glistening except for a 5 by 3 cm. area of opacity in the visceral layer covering the anterior part of the right ventricle. The usual amount of clear, pale yellow fluid was contained within the pericardial sac.

Aorta: The intima showed only a few small atheromatous plaques in the abdominal segment. The wall of the ascending aorta was moderately thickened and several white, waxlike plaques were seen on the intimal surface.

Heart: The myocardium was very flabby and uniformly soft and reddish brown. Both ventricles were slightly dilated; the auricles were filled with cruor. On the tricuspid leaflets, near the free margin there was a 1 by 1 cm. firm, friable, yellow mass closely adherent to the underlying valvular endocardium. The pulmonary valve showed no abnormalities. The mitral valve was thin, smooth, flexible and of average length, and there was nothing suggestive of vegetations. The papillary muscles were of average size; the chordae tendineae were not shortened or fused together. On the anterior cusp of the aortic valve there was a yellowish green, homogeneous, friable mass measuring 1.5 by 1 by 1 cm., which was firmly adherent to the ventricular surface of the valve. The remaining two cusps showed several firm white nodules measuring approximately 1 by 1 mm., arranged along the line of closure. The coronary vessels were free from any significant atherosclerosis.

Lungs: The consistency of both lungs was somewhat increased throughout but the left lower lobe was distinctly consolidated. The cut surfaces of the right lung and left upper lobe were hemorrhagic, and a great deal of blood tinged fluid escaped when pressure was made on the lung parenchyma. The left lower lobe on section was somewhat dry and more granular than the cut surfaces of the other lobes. The bronchial mucosa was hyperemic and edematous. The pulmonary vessels contained no thrombi. There was no evidence of suppuration in any portion of either lung. The regional lymph nodes were not remarkable.

Spleen: The spleen was greatly enlarged and so soft that on sectioning the pulp was almost semifluid. The capsule was thin, smooth and slate gray; the pulp was uniformly purplish red. The follicles and trabeculae could not be distinguished.

Kidneys: Both organs were moderately enlarged, of average firmness and cut with normal resistance. The capsules stripped

Genitalia: The uterus measured 5 by 6 by 3 cm.; it cut with the usual resistance. The endometrium averaged 2 mm. in thickness and was uniformly dark red. The fallopian tubes were tortuous, bound down by fibrous adhesions and in several places were moderately dilated. The ovaries were small, firm, white and fibrous.

Gastrointestinal Tract: The peritoneal surfaces were smooth and pale gray. The stomach contained a small amount of gray opaque fluid. The mucosa was smooth and pallid and showed numerous petechiae. The lumen of the large and small intestine was of average size and the contents were not abnormal. The mucosa was intact throughout and essentially normal in appearance. The mesenteric blood vessels showed no change.

TABLE 2.—*Urinalyses*

Date	Specific Gravity	Reaction	Albumin	Sugar	Microscopic Observations
3/31/40	1.020	Acid	Negative	Negative	Occasional leukocytes
4/ 5/40	1.016	Alkaline	Negative	Negative	Occasional leukocytes; occasional epithelial cells

Liver: This organ was enlarged, moderately soft and uniformly yellow. Resistance to cutting was somewhat decreased and the cut surface was uniformly pale yellow and soft with indistinct markings.

Gallbladder and Ducts: The gallbladder was slightly distended by 25 cc. of light amber colored bile which flowed readily through the ducts and from the ampulla of Vater. The wall was moderately thickened, and attached to the mucosa were numerous orange granules which in some places formed definite ridges. The bile ducts were not dilated and contained no calculi.

Pancreas: This organ was of average size, shape and consistency. It was a yellowish brown, firm and distinctly lobulated. The surrounding fat was of average amount and of the usual color. The pancreatic ducts appeared normal.

Adrenals: Both adrenals were of average size, shape and consistency. The medullary portions were a gray brown and firm. The cortical layers were dark brown instead of the usual deep yellow.

Vertebrae: The cancellous portion of the bodies contained uniformly pale red marrow.

Chemical Examination of the Concretions.—The kidney calculi on chemical examination were found to consist of acetyl-sulfathiazole to the extent of about 50 per cent of the dry weight. A slight trace of free sulfathiazole was present.⁵

SUMMARY AND COMMENT

Sulfathiazole concretions were found in the kidneys, ureters and bladder of a patient treated for pneumonia with sulfathiazole who did not present any evidence of disturbance of the urinary tract. It is therefore of clinical importance to study the effects of sulfathiazole on the kidneys so as to determine whether sulfathiazole crystals are nonirritating to the kidneys or whether there is a latent period between the formation of crystals in the urinary tract and the development of kidney insufficiency. If sulfathiazole crystals can remain in the kidneys, ureter and bladder without causing early clinical signs of renal damage, it will be desirable to determine its ultimate effect on the kidneys by studying the renal functions of patients, who were treated with the drug, for a period of one year after the drug has been discontinued.

Sulfathiazole in this case had no effect on the pneumococcemia or on the acute bacterial endocarditis.

How frequently crystallization of sulfathiazole may occur in the urinary tract is as yet unknown. Of sixteen autopsies reported by Flippin⁶ on patients treated with sulfathiazole, none showed uroliths, though among the hundred or more patients treated with that drug there were quite a few who had mild urinary disturbances.

1905 Spruce Street.

5. This examination was by J. G. Reinhold, Ph.D., chief biochemist to the laboratory of the Philadelphia General Hospital.

6. Flippin, Harrison F.: Personal communication to the authors.

TABLE 1.—*Blood Counts*

Date	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Poly-nuclears, per Cent	Staff Cells, per Cent	Segmented Forms, per Cent	Lymphocytes, per Cent	Mono-cytes, per Cent
3/31/40	68	3,100,000	19,200	80	18	2
4/ 1/40	68	3,320,000	16,400	76	64	12	12	12
4/ 3/40	68	3,200,000	18,400	92	82	10	8	..
4/ 8/40	52	2,600,000	13,000	74	58	16	10	10

with ease, revealing a smooth pale red surface. On section the cortex was found to be from 1 to 1.5 cm. in width, of a uniform pale red and indistinctly demarcated from the medulla. In the calices and pelvis there were numerous bright orange colored irregular shaped calculi measuring from 1 to 2.5 mm. in diameter. The pelvis were not dilated and the mucosa was uniformly smooth and moderately hyperemic.

Urinary Tract: The serosal surfaces were smooth and pale pink. The ureters were slightly dilated and contained numerous granules similar to those found in the calices. The left ureter near its source was almost completely occluded by a mass of the same type of orange colored calculi. The bladder was small and contracted; the mucosa was slightly hyperemic, and attached to its surface were several granular masses similar to those noted in the ureters and pelvis.

CONGENITAL HYPERTROPHY OF THE VERUMONTANUM

FREDERICK PILCHER JR., M.D., AND HAROLD W. PRICE, M.D.
CALGARY, ALTA.

Congenital hypertrophy of the verumontanum is one of the rarest lesions in the posterior urethra. A case in which this anomaly was discovered at autopsy led us to a thorough review of the literature, which disclosed only thirteen previously reported cases. In the case recorded here the lesion was somewhat different from any of those observed.

REPORT OF CASE

A. P. D., a white boy, was born at the Calgary General Hospital on July 2, 1937. This was the mother's second pregnancy. A previous and a subsequent child are both normal and well. Pregnancy and delivery were normal. The birth weight was 8 pounds 10½ ounces (3,926 Gm.). Routine physical examination after birth disclosed nothing abnormal. After the usual postnatal drop in weight the child began to gain normally. On the sixth day there were fever and diarrhea, but these lasted



Fig. 1.—Entire urinary tract showing the dilated kidneys, tremendous dilatation of the ureter and thickened hypertrophy of the bladder.

only two days. Thereafter his progress was normal and uneventful. The child and mother left the hospital on the fourteenth day and went home to the country.

On July 22 the child was brought back to the city by his mother. He had nursed poorly, had not taken his bottle well and on the day of examination had refused to take anything by mouth. The child was markedly emaciated and moribund. The abdomen was soft and scaphoid, and peristaltic waves were visible. Both kidneys were easily palpable and larger than normal. Otherwise examination was negative. The child was sent to the hospital, where subcutaneous fluids were administered. He died five hours after admission.

Autopsy performed by Dr. Lola McLatchie showed marked emaciation and pale dry tissues. Complete examination was otherwise essentially negative except for the urinary tract. The illustrations show clearly the appearance of the fixed specimen. Both kidneys were full of thick purulent urine. The

From the Calgary Associate Clinic.

markedly enlarged and elongated verumontanum projected into the bladder. Lifted forward, the verumontanum acted as a valve which completely or almost completely occluded the urethra. There was no other obstruction in any part of the urethra.

LITERATURE

The three congenital obstructive lesions observed in the posterior urethra are valves, contractures and hypertrophy of the verumontanum. According to the literature, valves are the



Fig. 2.—A clearer view of the elongated hypertrophied verumontanum.

most common and hypertrophy of the verumontanum the least common. Young, Frontz and Baldwin¹ in 1919 presented the first thorough review of congenital valves in the posterior urethra. Since then, painstaking reviews of the literature and reports of personal cases have been published by numerous authors. In none of these papers, however, is hypertrophy of the verumontanum mentioned as the sole cause of obstruction. In the presence of valves there often is observed a variable



Fig. 3.—Section through the elongated verumontanum and region of the bladder neck; reduced from a photomicrograph with a magnification of 9 diameters.

degree of enlargement or distortion of the verumontanum, but the valves act as the obstructing agent. Enlargement of the verumontanum alone as the cause of obstruction was first

1. Young, H. H.; Frontz, W. A., and Baldwin, J. C.: Congenital Obstruction of the Posterior Urethra, *J. Urol.* 3: 289-354 (Oct.) 1919.

reported by Bugbee and Wollstein² in 1923. They observed seven cases at autopsy and one clinical case. All but two of the patients were under 1 year of age and the oldest was 3½ years. Robinson³ in 1927 reported an autopsy specimen from a man aged 19. Dodson and Lorraine⁴ observed during life a youth aged 19 in whom hypertrophy of the verumontanum was a cause of urinary obstruction and retention, and a good result followed fulguration of the verumontanum. Baldrige⁵ reported another case in which cure followed fulguration of the verumontanum in an 11 year old patient. Somerford⁶ in 1936 again observed this lesion at autopsy in a child aged 11 years. The latest report is that of Grant⁷ in 1938 in which he mentions a boy aged 13 years in whom hypertrophy of the verumontanum was noted during life and relief of obstruction followed fulguration of the verumontanum.

COMMENT

There is no satisfactory explanation for congenital hypertrophy of the verumontanum. The greatly enlarged verumontanum probably acts as a ball valve just in front of the external sphincter in the same way that median lobe prostatic hypertrophy acts in the region of the internal sphincter. Mechanical obstruction to the flow of urine is produced.

The pathologic changes in the urinary tract and the symptoms are similar to those resulting from enlargement of the prostate gland or any other type of infravesical obstruction. There is dilatation of the posterior urethra behind the verumontanum. During the earlier stages of obstruction there are hypertrophy of the bladder with trabeculation, hypertrophy of the trigon, perhaps diverticulum formation and inflammation, dependent on the degree of associated infection. Later, when decompensation of the bladder occurs, there follows dilatation of the bladder, which together with inflammatory changes in the bladder wall result in incompetence of the ureterovesical valve mechanism. Ureteral and pelvic dilatation occur, and in the most advanced cases the renal parenchyma becomes a thin shell. This compression atrophy, accompanied in many cases by infection, eventually reduces renal function to a point at which it will no longer support life.

The early symptoms are those of urinary obstruction. Later there are renal insufficiency and uremia. Frequency of urination is the most common symptom. With associated infection, frequency often becomes very marked with almost constant dribbling. Enuresis may be the most prominent symptom. One may observe in older children considerable straining, hesitancy and difficulty in voiding. When bladder distention occurs it may be observed as a mass in the lower part of the abdomen. Recurrent episodes of fever, often diagnosed as pyelitis, are common. As renal damage advances, the symptoms of renal insufficiency appear. There may be failure to gain, or even loss of weight. Loss of appetite and gastrointestinal upsets are common, as well as headaches and lassitude. With a lowered renal reserve these patients are more susceptible to intercurrent infections and often die of them. They may lapse into uremic coma. The true cause of the trouble may never be suspected, and the patient is often treated for pyelitis or chronic nephritis.

The diagnosis is established by making thorough urologic examination of all children who have chronic urinary troubles. Urethroscopic examination of these children will differentiate contractures, valves, hypertrophy of the verumontanum and cord bladder.

The treatment consists in removal of the obstruction when the condition of the patient permits. Infection and renal impairment may necessitate preliminary urethral catheter or suprapubic drainage for a variable length of time. Abundant

fluids and urinary antiseptics will hasten improvement. Blood transfusion is indicated in the anemic and those in generally poor condition. The hypertrophied verumontanum may be destroyed by any of the various punch instruments or by simple fulguration through the cysto-urethroscope.

SUMMARY

The congenital hypertrophy of the verumontanum here reported is of unusual configuration. This is one of the rarest obstructive lesions in the posterior urethra. A thorough review of the literature discloses only thirteen previously recorded cases. With careful attention to urinary symptoms and thorough urologic examination, this lesion should be discovered before renal damage has progressed to a point at which recovery is impossible. Treatment consists in proper preoperative preparation of the patient, followed by transurethral punch or fulguration of the verumontanum.

214 Sixth Avenue West.

Special Article

GLANDULAR PHYSIOLOGY AND
THERAPYCORTICOTROPIC (ADRENOTROPIC),
THYROTROPIC AND PARA-
THYROTROPIC FACTORS

JAMES B. COLLIP, M.D.

MONTREAL, CANADA

This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—Ed.

THE CORTICOTROPIC FACTOR

It is to be noted that the word "corticotropin" (or "corticotrophin") is now being widely used as a descriptive term for the principle in the anterior lobe of the pituitary gland hitherto commonly spoken of as the adrenotropic factor. This is in line with the general recommendations of the Third International Conference on the Standardization of Hormones.¹

Physiologic Significance of Corticotropin.—There is now a mass of evidence that the maintenance of the cortex of the adrenal gland, in the morphologic as well as the functional sense, is dependent on the secretory activity of the normal anterior lobe of the pituitary. The atrophic adrenals of the completely hypophysectomized animal are not entirely functionless, however, since removal of them from rats hypophysectomized some weeks previously is not tolerated, and death ensues quickly. The function of the corticotropic factor is therefore to maintain the normal structure and function of the adrenal cortex.

Nature of the Corticotropic Factor.—Until such time as the hormones secreted by the anterior lobe are obtained in pure form, it will be impossible to know positively whether the substance acting on the adrenal cortex is a single substance having only this specific hormonal activity or a substance having other physiologic effects, tropic or otherwise, in addition to the

2. Bugbee, H. G., and Wollstein, Martha: Retention of Urine Due to Congenital Hypertrophy of the Verumontanum, *J. Urol.* **10**: 477-490 (Dec.) 1923.

3. Robinson, W. W.: Congenital Hypertrophy of the Verumontanum as a Cause of Urinary Retention, *J. Urol.* **17**: 381-390 (March) 1927.

4. Dodson, A. I., and Lorraine, Helen: Congenital Obstruction of the Posterior Urethra, *Virginia M. Monthly* **58**: 102-107 (May) 1931.

5. Baldrige, R. R.: A Case of Congenital Hypertrophy of the Verumontanum, *New England J. Med.* **213**: 46-49 (July 11) 1935.

6. Somerford, Anne E.: Congenital Urethral Obstruction, *Lancet* **1**: 1473 (June 27) 1936.

7. Grant, Owsley: Obstructions at the Vesical Neck in Children, *J. Urol.* **40**: 114-120 (July) 1938.

From the Department of Biochemistry, McGill University.

1. Report of the Third International Conference on the Standardization of Hormones, *Bull. Health Organ. League of Nations* **7**: 887-899 (Oct.) 1938.

corticotropic property. Collip² reported that an isoelectric protein fraction obtained from an acid acetone extract had the properties of three hormones of the anterior lobe, namely, the growth-promoting factor, corticotropin and prolactin. The corticotropic activity of such extracts was shown to be fairly resistant to heating over a wide p_H range; the greatest stability was shown at p_H 3 to 5. Moon,³ using the Lyons method⁴ for the preparation of prolactin, showed that the material insoluble at p_H 6.5 is rich in corticotropin. This fraction had little prolactin activity, whereas a fraction obtained by isoelectric precipitation at p_H 5.5 was rich in prolactin but had a lower corticotropic content. It can be positively stated that corticotropin is separate and distinct from thyrotropin and from gonadotropin.⁵ All available evidence points to corticotropin being of protein nature.

Preparation of Potent Extracts of Corticotropin.—Although it has been my experience that most protein fractions obtained from extracts of anterior lobes have more or less corticotropic activity, I have found the following method satisfactory for the preparation of an extract rich in corticotropin and having a minimum of other principles of the anterior lobe.

Prime fresh tissue which has been largely defatted and dehydrated by extraction with alcohol is extracted twice with 5 volumes of 0.25 per cent acetic acid for each volume of original gland tissue used. The residues are then extracted a third time with 5 volumes of 0.25 per cent acetic acid, the mixture being heated to 75 C. for fifteen minutes, then cooled and filtered. The tissue residues are then suspended in 5 volumes of 0.25 per cent acetic acid and placed in a boiling water bath for four to six hours, the mixture being frequently stirred. The mixture is then filtered, and the filtrate is concentrated at low temperature and pressure until the volume is equal to the original volume of gland used. Sufficient concentrated hydrochloric acid is then added to make a 0.25 per cent concentration of this reagent, and the acidified mixture is placed in a boiling water bath for twelve hours. The extract at this stage is adjusted to p_H 4 and is ready for assay on the hypophysectomized rat. The salt content can be reduced by a short dialysis in cellophane. Fractionations of such extracts with a view to obtaining the corticotropic principle in purer form are being undertaken. An earlier observation that extracts obtained from simple hydrolysates of pituitary tissue (treatment on a boiling water bath for twelve to twenty-four hours with 10 volumes of 0.25 per cent hydrochloric acid) produced a number of physiologic effects when tested in the appropriate manner suggested the process described here for the preparation of extracts of corticotropin. In addition to retaining corticotropic properties, these simple hydrolysates were found to contain appreciable amounts of the metabolic, glycotropic and ketogenic substances. Feeding of hypophysectomized rats with such potent preparations has given no evidence that the corticotropic substance is active when taken orally.

Bioassay for the Corticotropic Substance.—In my opinion the most satisfactory method of assay for corticotropin is by the use of hypophysectomized rats. These animals should not be used until an adequate time has elapsed after hypophysectomy to insure that cortical atrophy has progressed to a marked degree. One month is a safe interval. In the method of assay originally described,⁶ one adrenal was removed from the test animal prior to beginning injections of the extract to be assayed. This was weighed and sectioned, and served as the control.

The injections were made twice a day for six days, and then the remaining adrenal was removed, weighed and sectioned for histologic study. It was suggested that a 50 per cent increase in weight together with positive histologic evidence of cortical repair should be considered a unit effect. A more extensive study of the response of hypophysectomized rats to a single corticotropic preparation administered at increasing levels of dosage showed that the accurate assay of such extracts for corticotropin is a very difficult matter.⁷ It is now believed that much greater uniformity can be obtained if restoration to normal or nearly normal size of the adrenals is accepted as a unit effect. It is suggested also that the period of injections be increased to ten days, that several animals be used and that biopsy is unnecessary.

The method of Moon³ for the assay of corticotropin consists in the treatment of normal 21 day old male rats for three days with the extract to be tested. Moon defined a unit as that amount of extract tested in this manner which caused a fifty per cent increase in the weight of the adrenals. An inert protein solution is used as a control in the Moon test. The Moon method of assay has much to commend it, and in the case of purified extracts there should be little danger of non-specific effects being obtained, for it is well known that adrenal enlargement due to cortical hypertrophy is readily obtained by treatment of normal rats with injections of a foreign protein.

General Considerations.—The ability of the normal anterior lobe to secrete corticotropin quickly in increased amounts in response to a great variety of so-called nonspecific agents would seem to constitute one of the chief arms of defense on the part of the body to injurious stimuli.⁸ As yet no success has been had in the demonstration of corticotropin in the blood. It would be of clinical value if more sensitive methods for the detection of this substance were available, so that actual assays of blood and urine in cases of Cushing's disease could be made.

No specific clinical value for preparations containing corticotropin has been demonstrated. There is the possibility that they might be of definite prophylactic value in cases of anticipated shock. There is likewise the possibility that in certain cases of Addison's disease there might be benefit from this form of therapy. Presumably, although there is no direct proof of it, the corticotropic substance causes the adrenal cortex to function to the full measure of its capacity. I have observed that the activity of hypophysectomized rats as measured in the running wheel cage is greatly increased after prolonged treatment with corticotropic extract. In view of the important, though as yet none too well defined, role which the adrenal glands play in carbohydrate and protein metabolism, as well as other phases of metabolism, a very important place must be assigned to the corticotropic hormone among the family of active principles of the anterior lobe.

THE THYROTROPIC HORMONE

Since the publication of the last edition of "Glandular Physiology and Therapy," in which knowledge of the thyrotropic hormone was reviewed, numerous papers have appeared dealing with this subject, but, as Van Dyke remarked in his excellent review of the physiology and pharmacology of the pituitary gland,⁹ recent investigations of the thyrotropic hormone from various biologic standpoints have yielded a disappointingly small crop of facts. Much of the effort has been expended in consolidating or extending slightly knowledge which was already available.

2. Collip, J. B.: Properties of Anterior Lobe Extracts, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, 1937, vol. 5, pp. 210-217.

3. Moon, H. D.: Preparation and Biological Assay of Adrenocorticotrophic Hormone, *Proc. Soc. Exper. Biol. & Med.* 35: 649-652 (Jan.) 1937.

4. Lyons, W. R.: Preparation and Assay of Mammatropic Hormones, *Proc. Soc. Exper. Biol. & Med.* 35: 645-648 (Jan.) 1937.

5. Collip, J. B.; Anderson, E. M., and Thomson, D. L.: The Adrenotropic Hormone of the Anterior Pituitary Lobe, *Lancet* 2: 347 (Aug. 12) 1933.

6. Collip, J. B.: Some Recent Advances in the Physiology of the Anterior Pituitary, *J. Mt. Sinai Hosp.* 1: 28-71 (May-June) 1934. Collip.²

7. Collip, J. B.: Results of Recent Studies on Anterior Pituitary Hormone, *J. Biol. Chem.* 45: 782-804, 1938.

8. See adrenals in the Response of the Organism to Stress, *Brit. J. Exper. Path.* 17: 234-245 (June) 1936.

9. Van Dyke, H. B.: The Physiology and Pharmacology of the Pituitary Body, Chicago, University of Chicago Press, 1939, vol. 2.

Heyl and Laqueur¹⁰ expressed the view that the principle responsible for thyroid enlargement differs from that which causes the histologic signs of hyperplasia. Heyl¹¹ emphasized that certain pituitary extracts cause obvious histologic signs of thyroid stimulation without increasing the weight of the gland, while other extracts elicit a pronounced increase in weight. He isolated a protein-free acetone-soluble pituitary fraction which had no effect on the thyroid by itself but caused marked enlargement of the gland when given in combination with a highly purified thyrotropic preparation that in itself caused only histologic signs of hyperplasia. He concluded that, in addition to the thyrotropic hormone, the hypophysis produces an activator responsible for the increase in weight. More recently, Billingsley,¹² studying this question in my laboratory, summarized his results as follows:

A number of thyrotropic extracts have been simultaneously assayed by the weight and histology of the guinea pig thyroid, and by the metabolic rate. No correlation can yet be expressed between these, except that increase in weight and hyperplasia apparently are associated more often than are either of these responses with an increased metabolism. The metabolic rate was found to respond most readily to thyrotropic extracts, and the guinea pig was more sensitive than the hypophysectomized rat. The anterior pituitary appears to have a two-fold action on the thyroid: one which influences the secretion of the thyroid hormone, the other to change the morphology of the gland. It is doubtful whether an identical mechanism is involved in each case, as indicated by comparative studies of the three assay methods.

Relations of the Thyrotropic Hormone to Other Hypophysial Principles.—Riddle and his co-workers¹³ showed that active gonadotropic pituitary preparations tested in pigeons do not always exert a thyrotropic effect. This indicates that the two hormones are not identical. Yet more recently, Tolksdorf and Jensen¹⁴ and Jensen and Tolksdorf¹⁵ came to the conclusion that the thyrotropic factor is identical with the interstitial cell-stimulating, or luteinizing, factor, since all pituitary fractions containing thyrotropin proved also to be active luteinizers and vice versa. Since purified thyrotropic preparations do not inhibit the action of insulin in the mouse, Jensen and Grattan¹⁶ concluded that the glycotropic action is not due to the thyrotropic principle, thus confirming the view of Young.¹⁷

Mechanism of the Thyrotropic Action.—Schneider¹⁸ and Schneider and Widmann¹⁹ observed that in the dog an extract containing thyrotropin increases the iodine content of the blood without a period of latency, thus differing from the action of thyroxine. Similarly in the guinea pig it leads to a rapid appearance of signs of

thyrotoxicosis. Although these signs are not evident before the thyroid undergoes hyperplasia, they develop much sooner than after treatment with thyroxine. These experiments suggest that the actions of the thyrotropic principle cannot be regarded as due merely to a liberation of thyroxine.

The fact that the thyrotropic hormone acts directly on the thyroid without any intermediary has been demonstrated by Eitel and his associates,²⁰ who found that an extract containing this factor when added to slices of dog thyroid increased the consumption of oxygen by the thyroid tissue and caused histologic changes similar to those usually seen in vivo.

Bioassay for the Thyrotropic Substance.—The Third International Conference on the Standardization of Hormones¹ agreed that extracts of the thyrotropic factor should be assayed in comparison with an international standard preparation which is distributed by the National Institute for Medical Research, Hampstead, London, England; 250 micrograms of this preparation are equivalent to 1 unit. It also agreed that only those tests can be considered safe which are based on actual observation of a stimulation of the thyroid, since other effects may be due to impurities in the extract.

In the axolotl, preparations of the thyrotropic substance induce metamorphosis, and this effect has been suggested as a basis for the assay of extracts for the thyrotropic principle.²¹

The frog tadpole has been used for the assay of preparations for the thyrotropic substance by Cuyler and co-workers,²² who standardized such preparations on the basis of an accelerating effect on metamorphosis.

The grass snake (*Tropidonotus natrix*) is a particularly good test object, according to Mason,²³ because its thyroid, unlike those of laboratory rodents, shows surprisingly little variation from the normal resting condition unless stimulated by pituitary extracts. The disadvantage of this method is that few laboratories are equipped with this experimental material.

The thyroid of the pigeon or of the dove likewise undergoes pronounced enlargement and shows histologic signs of hyperplasia after administration of an extract containing thyrotropin and is a suitable test object for assay purposes. It is important, however, to use either immature²⁴ or hypophysectomized²⁵ birds in order to make sure that the untreated controls have resting thyroids.

Immature chicks were first employed for such bioassays by Stimmel and associates,²⁶ who considered the decrease in the iodine content of the thyroid caused by the thyrotropin in an extract as an indicator of activity. Later Smelser²⁷ and Cope²⁸ used the increase in the weight and the histologic signs of hyperactivity elicited by the thyrotropic factor in the 1 day old chick as a basis for bioassay. Kabac and Liapin²⁹ made an accurate detailed study of this test object, using 5 to 6 day old chicks and estimating thyrotropic potency merely by the increase in thyroid weight. They stated: "As an arbitrary unit of thyrotropic preparation we designate the amount which brings

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12. Billingsley, L. W.: Factors Affecting the Metabolism of Small Animals, Thesis, McGill University Graduate School, 1937.

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18. Schneider, E.: Morbus Basedow und künstliche Steigerung der Schilddrüsenaktivität, Arch. f. klin. Chir. 173: 421-428, 1932.

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22. Cuyler, W. K.; Stimmel, B. F., and McCullagh, D. R.: Quantitative Studies with Thyrotropic Hormone, J. Pharmacol. & Exper. Therap. 58: 286-293 (Nov.) 1936.

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24. Riddle, Oscar: Studies on Pituitary Functions, Endocrinology 15: 307-314 (July-Aug.) 1931.

25. Miller, R. A., and Riddle, Oscar: Stimulation of Adrenal Cortex of Pigeons by Anterior Pituitary Hormones and by Their Secondary Products, Proc. Soc. Exper. Biol. & Med. 41: 518-522 (June) 1939.

26. Stimmel, B. F.; McCullagh, D. R., and Picha, Valerian: The Thyrotropic Hormone of the Pituitary Gland and Iodine Metabolism, J. Pharmacol. & Exper. Therap. 57: 49-55 (May) 1936.

27. Smelser, G. K.: Assay of Thyrotropic Hormone on Day-Old Chicks, Proc. Soc. Exper. Biol. & Med. 37: 388-390 (Nov.) 1937; Chick Thyroid Responses as a Basis for Thyrotropic Hormone Assay, Endocrinology 23: 429-438 (Oct.) 1938.

28. Cope, C. L.: The Young Chick as Test for the Thyrotropic Hormone, J. Physiol. 94: 358-364 (Dec.) 1938.

29. Kabac, J. M., and Liapin, N. I.: A Quantitative Study of the Thyrotropic Action of Extracts of Anterior Pituitary on Chicks, Bull. de biol. et de méd. expér. de l'U. R. S. S. 5: 334-338 (April) 1938.

the weight of both thyroids of the chick to 8 mg. (on the average) after daily subcutaneous injections during five days. The experiments were carried out on 5 day old chicks, and autopsy was performed one day after the last injection." Bergman and Turner,³⁰ who employed the 1 day old white leghorn chick, emphasized that males are more sensitive than females. They defined the unit of thyrotropic activity as the total amount of extract administered subcutaneously once daily during four days which will cause a mean increase of 50 per cent (to about 5.4 ± 0.26 mg.) in thyroid weight in 20 chicks whose body weights average 55 ± 10 Gm. This unit corresponds to about one quarter of the guinea pig unit employed by the same investigators.

The guinea pig is the most commonly employed test object for thyrotropin. It represents an excellent test object, but a relatively young animal must be used in order to insure that the thyroid is in the resting stage before the thyrotropic preparation is administered. Aron³¹ and Aron and Klein³² stated that this is always the case in animals weighing less than 250 Gm. Loeser³³ used guinea pigs weighing 180 to 220 Gm. However, several subsequent investigators found that even in the small animal the thyroid may show signs of hyperplasia and of absorption of colloid under apparently normal conditions.³⁴ This variability of the normal thyroid structure induced Benazzi³⁵ and Junkman and Schoeller³⁶ to employ only animals weighing between 100 and 150 Gm. Aron³⁷ insisted, however, that the 200 Gm. guinea pig is suitable for assay purposes. He defined the unit as $\frac{1}{400}$ of the amount necessary to produce a 50 to 100 per cent weight increase in the thyroid of a 200 Gm. guinea pig twenty-four hours after this amount is administered in a single injection. Histologically, 100 units causes absorption of colloid and secretory phenomena in the enlarged acinous cells throughout the glandular parenchyma. Ten units exerts such an effect only in the central portion of the gland; 40 to 45 units represents the amount which is most easily gaged in a single test since it causes absorption of colloid, hyperplasia and the appearance of mitotic figures, but none of these signs is sufficiently marked to make it impossible to differentiate the effect from that of still higher doses. Well aware of the variability of the thyroid even among young normal guinea pigs, Paal and Kleine³⁸ described a "resting diet" which causes the thyroid to become entirely free of any signs of activity and thus makes it particularly suitable for bioassay purposes. De Fremery³⁹ advocated pretreatment with the thyroid depressing diiodotyrosine for the same reason. Krogh and associates⁴⁰ emphasized that a few vacuoles in the colloid of the thyroid gland cannot be considered as significant, and this is in agreement with my own observations. However, if this is kept in mind, 200 Gm. guinea pigs are quite suitable

for assay purposes, unless extremely small doses have to be detected. Such guinea pigs have also been used by Rowlands and Parkes,⁴¹ who adopted as a unit "the thyrotropic activity contained in an amount of extract which given daily for 5 days will cause the thyroids of the 200 Gm. guinea pigs to attain a weight of 60 mg., i. e., about double the normal." This method of assay has been accepted by Junkman and Loeser.⁴² Starr and Rawson,⁴³ Rawson and Starr⁴⁴ and Starr and others⁴⁵ measured the height of the thyroid epithelium and found it to be about 3.75 microns in normal females weighing 180 to 225 Gm. Using this "microhistometric" method, they assayed urine for its thyrotropic activity in various diseases by the increase in epithelial height which it produces. Heyl and Laqueur⁴⁶ insisted that the histologic changes, namely, the increase in the epithelial height and the vacuolation of the colloid, are the only satisfactory indexes of thyrotropic activity. They worked out a scale of six different stages of histologic signs of activity which they designated by the letters p to u. They termed "borderline dose" the amount which when given in two intraperitoneal injections on two consecutive days will cause in two thirds of the treated 150-200 Gm. guinea pigs a reaction "s" in the middle part of the thyroid within forty-eight hours. This reaction "s" is defined as a thickening of the cells in which the nucleus becomes round and the protoplasm develops on the distal pole of the cell to about the width of the diameter of the nucleus. In order to keep their unit as close as possible to those generally in use, they defined 1 guinea pig unit as one quarter of the "borderline dose." Wilcke⁴⁶ pointed out that it is important always to use the same fixative, since Susa's—which causes practically no shrinkage—makes the cells appear higher than does ordinary solution of formaldehyde U. S. P. diluted 1:10. He claimed that for the Heyl and Laqueur test the latter fixative is preferable. More recently Bergman and Turner³⁰ defined 1 guinea pig unit as the total amount of an extract containing the thyrotropic factor which when administered subcutaneously once daily on five successive days causes a mean increase of 50 per cent (to about 26.4 ± 1.63 mg.) in the thyroids of 10 male guinea pigs whose weights average 155 ± 15 Gm. According to Bastenie and Zylberszac,⁴⁷ 0.025 mg. of colchicine given for every 30 Gm. of body weight to 220-250 Gm. guinea pigs makes the mitogenic action of the thyrotropic extract readily detectable, since colchicine arrests mitotic division in the metaphase. This drug should be administered about nine hours before killing the animals.

The decrease in the iodine content of the thyroid furnishes another test of thyrotropic activity in guinea pigs.⁴⁸

The thyroid of the mouse is generally not considered to be a suitable test object for bioassay purposes, although Paal and Kleine³⁸ claimed that by using a special diet one may sufficiently repress the thyroid even in this species to make the effect of thyrotropic evident.

The thyroid of the rat is normally too variable to be useful for bioassay purposes. In hypophysectomized animals, on the other hand, the restoration of the atrophic epithelium gives a good index for thyrotropic activity.⁴⁹ The low basal metab-

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olism of the rat is restored to normal by the thyrotropic factor, a change which has been advocated for bioassay purposes.⁵⁰ However, in view of the more recent discoveries showing that pituitary extracts other than those containing the thyrotropic principle may raise the basal metabolic rate, this method is not strictly specific.

Among other assay methods in which the rat is used should be mentioned that of Cuyler and co-workers,²² which is based on the action of the thyrotropic hormone in decreasing the iodine of the thyroid, and that of Karnofsky and Cronkite,⁵¹ based on the observation that this principle accelerates the eruption of the incisor teeth in the newborn rat.

Thyrotropic Content of Blood.—Van Caulaert and associates⁵² found that dog serum has the ability to stimulate the thyroid of the immature guinea pig. Fellingner⁵³ prepared an extract of dog blood which was definitely thyrotropic in the guinea pig.

Horse serum likewise shows thyrotropic activity.⁵²

Guinea pig blood, unlike that of most other species so far examined, does not contain any thyrotropic principle demonstrable by the guinea pig thyroid test.⁵⁴

Rabbit and rat blood are definitely thyrotropic in the guinea pig thyroid test.⁵² Aron⁵⁵ claimed that rat blood is particularly active in stimulating the thyroid of the immature rabbit.

Human blood is active in producing thyroid hyperplasia in immature guinea pigs.⁵⁶ Fellingner⁵³ showed that the active substance is readily extracted from the serum by 40 per cent acetone, from which it precipitates after the concentration is raised to 85 per cent. Aron⁵⁵ claimed that the thyrotropic activity may also be demonstrated by the effect of normal human blood on the thyroid of the immature rabbit.

Thyrotropic Content of Urine.—Emerson and Cutting⁵⁷ were unable to demonstrate any thyrotropic substance in dog urine using the guinea pig thyroid test. Similar negative results have been obtained with guinea pig urine by Aron,⁵⁴ who used the same test. Rat urine, on the other hand, is very active in stimulating the thyroid of the immature guinea pig.⁵⁸

Aron and collaborators⁵⁹ and Starr and associates⁴⁵ were able to demonstrate in the urine of man the presence of thyrotropic substance, using the thyroid of either the guinea pig or the rabbit as an indicator. Katzman and Doisy⁶⁰ stated that a modification of their tungstic acid process for the extraction of the gonadotropic factor from pregnancy urine is suitable for the extraction of a thyrotropic substance from urine. Nielsen⁶¹ claimed that the urine of some men stimulates, while

that of others depresses, thyroid development in the rabbit. Antognetti and Geriola⁶² and Emerson and Cutting⁵⁷ found normal urine quite inactive in the guinea pig thyroid test. Similarly, Jones⁶³ was unable to extract the thyrotropic principle from normal urine with a method which gave good recoveries when a pituitary extract containing this principle was simply added to urine. He concluded that either the hormone is not excreted in an active form or its chemical properties are so altered that it is not extractable with his method. Giedosz,⁶⁴ on the other hand, observed marked stimulation of the rabbit thyroid following administration of normal human urine. Sendrail and Tamalet⁶⁵ claimed that 15 cc. of normal urine (the amount employed for one 3 day assay) contains from 4 to 30 Aron guinea pig units.

Thyrotropic Content of Blood and Urine in Various Diseases.—In Simmonds's disease the thyrotropic activity of the urine is below normal as judged by the guinea pig thyroid test.⁶⁶

In acromegaly Fellingner⁵³ was able to recover thyrotropic substance in unusually large quantities from the blood, using his acetone extraction method. The urinary excretion of thyrotropic substance is increased in this disease, according to Nitzescu and Timus⁶⁷ and Sendrail and Tamalet,⁶⁵ who used the guinea pig thyroid test. The latter investigators obtained similar results in Cushing's disease. On the other hand, Jones,⁶³ who used the chick for assay, obtained negative results.

In myxedema and other types of hypothyroidism Aron,⁶⁸ Aron and Klein⁵² and Antognetti and Geriola⁶² obtained variable results, while Hertz and Oastler,^{49b} who followed restoration of the thyroid in hypophysectomized rats, and Rawson and Starr⁴⁴ and Sendrail and Tamalet,⁶⁵ who employed the guinea pig thyroid test, observed increased elimination of thyrotropic substance. Emerson and Cutting⁵⁷ using the latter test, found that following thyroidectomy the thyrotropic activity of the blood increases regularly, but such increase is only occasionally observed in spontaneous hypothyroidism. Jones,⁶³ who with his chick test could not detect any thyrotropic substance in the urine of normal persons or patients suffering from a variety of diseases, found a positive result in a case of myxedema.

The blood of patients with hypothyroidism is rich in thyrotropic substance, according to Fellingner,⁵³ Hertz and Oastler^{49b} and Bodart and Fellingner,^{66b} who also noted that following thyroidectomy the usually low thyrotropic activity of the blood of patients suffering from exophthalmic goiter undergoes a rapid and pronounced increase. It appears that the production of thyrotropic hormone is increased in thyroid insufficiency just as the output of gonadotropic hormone rises after the gonads are removed or have undergone involution.

In hyperthyroidism Aron^{68a} obtained variable results, while Krogh and Okkels⁶⁹ claimed that no thyrotropic activity can be demonstrated in the urine by the rabbit

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57. Emerson, Kendall, Jr., and Cutting, W. C.: Urinary Thyrotropic Hormone, *Endocrinology* **23**:439-445 (Oct.) 1938.

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66. Anderson and Collip.⁵⁰ Sendrail and Tamalet.⁶⁵

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thyroid test. Smith and Moore,⁷⁰ Antognetti and Gerioli,⁶² Emerson and Cutting,⁶⁷ Rawson and Starr,⁴⁴ Starr and other co-workers⁴⁵ and Sendrail and Tamalet,⁶⁵ all of whom used the guinea pig thyroid test, usually found subnormal quantities of thyrotropic substance in the urine, and in most cases this principle appeared to be entirely absent. Jones,⁶³ who used the chick test, likewise failed to detect excretion of thyrotropic substance. Drouet⁷¹ emphasized, however, that increased excretion of thyroxine, which may antagonize the effect of the thyrotropic hormone in the intact animal, may be the reason why most investigators were unable to detect the latter factor in the urine of hyperthyroid patients. He pointed out that negative results from urinary assays do not prove that thyrotropic substance is not excreted unless it is made certain that no substances antagonistic to the thyrotropic hormone are eliminated. It should be emphasized, however, that Hertz and Oastler,^{49b} who used hypophysectomized rats for their assays, were also unable to demonstrate thyrotropic activity in the urine of hyperthyroid patients, although in the absence of the pituitary the thyroid hormone would not have exerted an inhibitory effect. It is of interest, however, that, according to Nielsen,⁶¹ in exophthalmic goiter the urine actually causes atrophy of the epithelium in the rabbit thyroid, which suggests some antithyrotropic effect.

The blood of patients with hyperthyroidism likewise contains subnormal amounts of thyrotropic substance, according to the guinea pig assays of Fellingner⁵³ and Bodart and Fellingner.^{56b}

In obesity Merklen and co-workers⁷² invariably observed an increase in the elimination of thyrotropic substance, using the guinea pig test, while de Prat⁷³ obtained more variable results.

In various other diseases the results so far reported are too contradictory to justify detailed comment.⁷⁴ It is noteworthy, however, that, according to Aron,^{74a} in most cases the elimination curves of the thyrotropic and gonadotropic substances tend to run parallel.

Preparation of Active Extracts.—Greep⁷⁵ showed that a fairly complete separation of thyrotropic from gonadotropic substance could be obtained by treatment of extracts with benzoic acid. The thyrotropic factor was precipitated with the benzoic acid, and the gonadotropic factor remained in the filtrate.

Lambie and Trikojus⁷⁶ have recently described a method of extraction and purification of the thyrotropic principle. Collip⁷⁷ has found that, in addition to the thyrotropic substance which is obtained in primary dilute acetic acid extracts, an isoelectric protein fraction can be prepared from the gland residues which is highly potent in thyrotropic properties. Moreover, guinea pigs treated daily with the latter fraction may not show

resistance to it for many months. This is confirmatory of the results of Werner,⁷⁸ who found that thyrotropic extracts prepared by different methods differed widely in their ability to cause development of the refractory state in guinea pigs.

Effect of Iodine on Action of Thyrotropic Hormone.—Friedgood⁷⁹ has reported that the administration of sodium iodide to guinea pigs receiving an extract containing the thyrotropic factor caused a remission of the symptoms of hyperthyroidism. Anderson and Evans⁸⁰ observed that in guinea pigs potassium iodide may prevent the metabolic action of thyrotropic extracts (perhaps because it prevents the discharge of thyroxine) without interfering with the effect on the thyroid itself. Franck⁸¹ found in guinea pigs treated with an extract of the anterior lobe that the basal metabolism decreased after an initial increase. During the period of decreased basal metabolic rate the thyroid showed storage of colloid. This storage appeared simultaneously with an enlargement of the Golgi apparatus and was considered to be due to a special action of the thyrotropic principle. Iodine administered to such animals prevented both the initial rise and the eventual fall in the basal metabolic rate. According to Franck, extracts of the anterior lobe cause degranulation of the eosinophils and an increase in the number of basophils in the anterior lobe of the guinea pig. These effects are inhibited by iodine. He concluded that the basophils of the pituitary secrete a thyrotropic hormone which stimulates storage of colloid in the thyroid follicles. The secretion of this hormone is prevented by the administration of iodine.

THE PARATHYROTROPIC HORMONE

Although the existence of a parathyrotropic hormone has not been proved as yet and may be regarded as rather doubtful, certain clinical and experimental evidence now available concerning this question will be discussed.

Parathyroid Tumors.—Adenoma of the parathyroids has repeatedly been observed in association with hypophysial tumors,⁸² a fact which suggests that a close relationship exists between these two glands.

Hypophysectomy.—In the dog Aschner⁸³ was unable to detect any change in the parathyroids following ablation of the hypophysis, while Koster⁸⁴ claimed that the parathyroids were invariably subnormal in size. Housay and Sammartino⁸⁵ stated that degenerative lesions

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72. Merklen, P.; Aron, Max; Israel, L., and Jacob, A.: Tests histologiques de l'hyperfonctionnement préhypophysaire chez certains obèses, *Bull. et mém. Soc. méd. d. hôp. de Paris* **51**: 1402-1406 (Nov. 4) 1935.

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81. Franck, S.: Histophysiologie de la préhypophyse, *Prehypophyse et glande thyroïde soumises à l'action de l'iode*, *Compt. rend. Soc. de biol.* **125**: 569-573 (Feb. 26) 1937.

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85. Housay, R. A., and Sammartino, R.: Les parathyroïdes dans l'hyperthyroïdisme et le diabète, *Compt. rend. Soc. de biol.* **111**: 111-113 (Jan. 1937); Epithelkörperchen bei den Hypophysen- und Pankreasinsuffizienzen des Hundes, *Beitr. z. path. Anat. u. z. allg. Path.* **93**: 405-416 (July) 1934.

and necrosis of the parathyroids may be observed in 66 per cent of all hypophysectomized dogs, while they are seen in only 10 per cent of the normal controls. After lesions of the tuber cinereum they were noted in about 41 per cent of the cases.

In the rat Smith⁸⁶ claimed to have noted atrophy of the parathyroids following hypophysectomy.

Hypophysectomy and Pancreatectomy.—The degenerative changes which occasionally occur following hypophysectomy are much more commonly observed in the dog in which the pancreas is also removed. Mere removal of the pancreas, however, does not elicit such changes except in rare cases.⁸⁷

Hypophysial Extracts.—In the cat Anselmino and co-workers⁸⁸ claimed that the so-called parathyrotropic extracts of the pituitary cause hyperemia and histologic signs of increased activity in the parathyroids without actually increasing their size.

In the dog, following treatment with hypophysial extract, enlargement of the epithelial cells, follicle formation and hyperemia have been observed without enlargement of the total volume of the gland,⁸⁸ and the structural changes were often accompanied by hypercalcemia.⁸⁹ Recently Ham⁹⁰ reported changes supposedly characteristic of the parathyrotropic hormone in the parathyroids of dogs treated with pituitary extract.

In the guinea pig Anselmino and associates⁸⁸ also claimed to have seen parathyroid stimulation after the administration of pituitary extract.

In the dwarf mouse Kemp and Marx⁹¹ claimed to have seen parathyroid enlargement following administration of a preparation containing the growth-promoting factor of the anterior lobe.

In the rabbit Hertz and Kranes,⁹² Anselmino and associates⁸⁸ and Cattaneo⁹³ observed enlargement and changes after treatment with various pituitary extracts, which they interpreted as characteristic of the parathyrotropic hormone.

In the rat Anselmino and co-workers⁹⁴ claimed to have obtained particularly obvious parathyroid enlargement accompanied by hypercalcemia following treatment with their extract of the parathyrotropic factor, and Hoffmann and Anselmino⁸⁹ emphasized that the hypercalcemia is prevented by parathyroidectomy.

It should be emphasized, however, that the existence of the parathyrotropic hormone has by no means been proved.⁹⁵

Special Clinical Article

CHEMOTHERAPY IN UROLOGY

CLINICAL LECTURE AT NEW YORK SESSION

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As in all fields of medicine, the advent of sulfanilamide and its derivatives has been a welcome addition to the armamentarium of the urologist. Almost a decade ago chemotherapy in urology made its first real step forward with the use of the ketogenic diet in the treatment of infection of the urinary tract. This rather cumbersome therapeutic agent was shortly followed by the discovery that mandelic acid is of equal value and much easier to administer. These therapeutic measures depended for their effectiveness on a certain concentration of an organic acid in the urine at a pH level below 5.5. Even when the desired conditions were met, many infections did not respond to such therapy. It was evident that, when a gram-negative bacillus or *Streptococcus faecalis* was present, bacteriostasis was the rule and the organism could be eradicated. However, when *Staphylococcus aureus* or *albus*, *Micrococcus* or the hemolytic or green-producing streptococcus was present these agents were not effective in destroying the organisms. The need for an adjunct to the treatment of such urologic conditions was apparent and the early reports concerning the use of sulfanilamide and its derivatives have stimulated investigation in the field of infections of the urinary tract.

The effectiveness of the sulfonamide compounds in the treatment of bacterial infections has entirely changed the practice of therapy within a few years. Owing to the chemical reactivity of the parent substance, countless derivatives have been synthesized and their therapeutic action has been determined. It is not within the scope of this paper to go into the history of the development of these compounds. Neither is it possible to discuss the entire gamut of those derivatives of sulfanilamide which have been used in the treatment of urologic diseases associated with or caused by bacterial invasion.

Before the actual use of these compounds in urology is discussed, a word or two concerning the mode of action seems indicated. Undoubtedly a direct action on the organism does take place both in vitro and in vivo. In urology the actual presence of the drug in the urine in the free form undoubtedly is a factor in its effectiveness, and its presence in tissue fluids enables it to reach the deeper seated infections. Whether or not the sulfonamide compounds have any effect on the immune processes of the body has been a point of controversy. The body defenses are important and necessary factors in the final curative effects, but whether phagocytosis is truly stimulated by the administration of these drugs is not definitely known at this time. More recently the bacteria-destroying property of the drug has been attributed to the accumulation of hydrogen peroxide due to the inactivation of catalase by the drug.

Turning now to the discussion of the clinical aspects of the use of the sulfonamide compounds, the main factors influencing the results obtained are the type of

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88. Anselmino, K. J.; Herold, L., and Hoffmann, F.: Ueber die Wirkung des parathyrotropen Hormons des Hypophysenvorderlappens bei verschiedenen Tiertypen, Ztschr. f. exper. Med. 97:51-59, 1935.

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organism present, the type of case being treated, the mode of administration and dosage used, and the patient's ability to tolerate the drug as evidenced by signs of toxicity.

TYPE OF ORGANISM

Early in our work from experimental and clinical data my associates and I became aware of the fact that sulfanilamide and its more closely related derivatives, such as disulfanilamide, and sulfanilyl-sulfanilamide, were the gram-negative bacilli and the beta-hemolytic streptococcus. The same was true for azosulfamide. The organisms of the genus *Proteus* have always presented a most difficult problem. Because of their urea-splitting property, chemotherapy requiring acidification of the urine was usually of little value because of the difficulty in producing the desired acidity. The sulfonamide compounds have been most useful in treating infection produced by this organism because these drugs in most instances are more effective in an alkaline medium. *Staphylococcus*, *micrococcus* and *Streptococcus faecalis* were usually not affected by these drugs with the exception of dimethyldisulfanilamide, which has never been marketed in this country because of the too frequent complication of peripheral neuritis largely involving the motor nerves. The gonococcus was attacked with considerable ease in the properly managed infection, but in many instances "sulfanilamide-resistant" cases were reported and the need for an additional chemotherapeutic agent became apparent.

The early experimental work with sulfapyridine showed little advantage in the treatment of infections of the urinary tract caused by the gram-negative bacilli or the streptococci. However, it was of some value in the group caused by the staphylococci. Because of the early reports concerning its action on the pneumococcus we used it in the treatment of infection produced by a similar organism, the gonococcus. Its efficacy here was much greater than that of sulfanilamide.

More recently we have had the opportunity to use another derivative, sulfathiazole, in the treatment of infections of the urinary tract. Again the usual gram-negative bacilli are destroyed by its administration. Of great interest to all of us is the fact that this drug is effective in eradicating staphylococcus and micrococcus, which were so resistant to the other sulfonamide compounds. The beta hemolytic streptococcus does not respond as well and in only about 30 to 40 per cent of the early cases was *Streptococcus faecalis* destroyed. Recently Helmholz has shown experimentally that the level of the p_H of the urine in vitro has a marked effect on the bactericidal property of sulfathiazole against *Streptococcus faecalis*. At a p_H of 5.0 a concentration of from 25 to 50 mg. per hundred cubic centimeters destroys the organism. As the degree of acidity decreases, a greater concentration of the drug becomes necessary until, at a p_H of 7.5, 200 mg. per hundred cubic centimeters will do little more than produce some bacteriostasis. We have been able to confirm this clinically.

Sulfathiazole, however, is the drug *par excellence* in the treatment of gonorrhea. To date we have treated only a group of sixteen patients suffering with this disease, but in all of them the gonococcus has been effectively destroyed within one week of the start of the administration of sulfathiazole. In the usual case the discharge disappears within three or four days and the two glass test shows both glasses of urine to be clear macroscopically and microscopically. At this time

the prostate is massaged and, if the secretion shows evidence of infection, regular prostatic treatment is instituted consisting of massage, irrigations and instillations as needed. If the prostatic secretion is negative, it is rechecked in another two or three days and if it still does not show any evidence of infection no further examination or therapy to the prostate is indicated.

TYPE OF CASE

Knowing the exact pathologic condition present in each case of infection of the urinary tract is just as important as knowing the exact organism responsible for the infection. By no means do I wish to imply that each patient who presents himself with the complaint of burning and frequent urination should be submitted to an extensive urologic investigation. Beyond any doubt, from the history and the initial examination our clinical judgment will decide its need in most instances. However, if after one or two satisfactory courses of chemotherapy the desired improvement and cure have not been gained or if repeated reinfection occurs, we must make certain that we are not dealing with complicating pathologic conditions such as stone, tumor, obstruction, foreign body or deep seated infection producing cicatrization and scarring of some part of the urinary tract.

Experience has taught us that in the simple uncomplicated cases of infection of the urinary tract almost any of the sulfonamide compounds is effective in destroying the disease in more than 90 per cent of the cases. Interestingly enough, this holds for the cases in which the infection is in the kidney as well as in those cases in which it is confined to the bladder alone, provided there is no cicatricial deformity or complications previously described. Early in our efforts we noted the inhibiting effect of chronic prostatitis on the efficacy of urinary antiseptics. The percentage of cases in which cures are effected is reduced almost a half unless the prostatic infection is adequately treated at the time of the drug therapy. It is not the rule that any of the sulfonamide compounds is regularly useful in treating nonspecific prostatitis. In certain cases in which the infecting organism in the urine can also be recovered from the prostatic secretion, good results may follow sulfanilamide therapy. Little more need be said concerning the usual complicating pathologic conditions found and the treatment required in certain infections of the urinary tract. Stone, foreign bodies and tumors should be removed; obstruction should be relieved. Unless this is done, only rarely shall we find the sulfonamide compounds of any use in the treatment of associated infection.

When the infection in the kidneys is of long standing and considerable cicatricial deformity, and perhaps caliectasis, have been produced, the problem of therapy is considerably more difficult. As mentioned previously, the action of the drug depends on its presence and concentration in the body fluids as well as in the urine. However, many observers believe the latter fact is the most important and consequently to obtain a bacteriostatic or bactericidal action in the urine we must have a kidney functioning well enough to excrete the drug. An infected, poorly functioning kidney will be benefited only to the extent to which the drug can be excreted by it. A most interesting observation has been that the sulfonamide compounds, and particularly azosulfamide, may be administered in moderate dosage to such patients with little chance of injuring these poorly functioning kidneys. This is not true when using

mandelic acid or the ketogenic diet, as with the latter therapeutic agents function is usually more impaired and the treatment must be stopped. More recently we have been using some of the newer sulfonamide compounds, particularly sulfathiazole, and, much to our surprise, have found the last mentioned drug to be more effective in the chronic case of pyelonephritis in which the kidneys show the typical chronic inflammatory changes such as cicatricial deformity and caliectasis with slight to moderate reduction in function as evidenced by the excretory urogram.

MODE OF ADMINISTRATION AND DOSAGE

The sulfonamide compounds when given to man may be given orally or parenterally. These drugs are almost entirely eliminated in the urine, partly in a free state and partly in a conjugated form, as an acetylated compound. It is the free form which exerts the bacteriostatic and bactericidal effect. When given orally the rate of absorption of these drugs varies with different cases and with the drug used, but usually two or three days is required to establish equilibrium between the amount ingested and the amount excreted. Somewhat less time seems to be necessary when sulfapyridine or sulfathiazole is administered. In certain instances oral ingestion is impossible for various reasons, and in these cases parenteral injection has been of great value. Sulfanilamide powder may be prepared in an 0.8 per cent solution in physiologic solution of sodium chloride and given subcutaneously. In this way a patient may be given more than 100 grains (6.5 Gm.) of the drug daily with little difficulty. The sodium salt of sulfapyridine may be given intravenously and some observers have recently shown that sulfathiazole may be given in the same way. The intravenous use of these drugs is useful in building up rapidly an appreciable level of the drug in the blood, particularly for those patients who have difficulty in taking the drug by mouth. The disadvantage, however, is that while the concentration in the blood is built up rapidly it also decreases rapidly and frequent administrations are necessary if an adequate concentration is to be maintained.

Clinically I do not feel that determinations of the level of these compounds in the blood are necessary in the satisfactory handling of patients suffering with infections of the urinary tract. Many estimations have been made and only in rare instances have I seen concentrations more than from 5 to 6 mg. per hundred cubic centimeters with the dosage usually used. I believe that a greater concentration in the blood is rarely needed to destroy an existing infection.

In the field of infection of the urinary tract the oral and subcutaneous administrations are usually sufficient. Various dosage levels have been suggested by many observers. However, it has been my experience that in the majority of instances sulfanilamide and its more closely related derivatives need seldom be given in a dosage greater than 40 grains (2.6 Gm.) daily. This is given in equal doses four times a day. The ease of administration may be enhanced by supplementing each dose with a similar quantity of sodium bicarbonate. The addition of the latter drug may have an additional value in that Helmholz and Sickler have shown that the efficacy of sulfanilamide in the urine is increased at a pH level of 7.5. If sulfanilamide must be given parenterally, a somewhat greater dosage is advised, as previously mentioned.

Azosulfamide, while not as effective as sulfanilamide in equal doses, is of great value in urologic work. It is

given in a dosage of 60 grains (4 Gm.) daily and may have to be used over a somewhat longer period. Usually sulfanilamide or azosulfamide is given for a period of from eight to fourteen days. At the end of that time we have deemed it advisable to stop the drug whether the urine has been sterilized or not. An intervening period of two or three weeks followed by a second course of the medication will frequently bring about the desired results. In a number of cases we have found a second and third course of the drug necessary before sterilization takes place.

Sulfapyridine has not been used extensively in this country in the treatment of the usual bacillurias and cocciurias. Foreign observers report little advantage for it over sulfanilamide in such cases. However, in the treatment of gonorrhea it has been of great value. We have regularly used a dosage of 45 grains (3 Gm.) daily for a period of from ten to fourteen days. If the urine in such cases is not grossly clear and the urethral discharge is not stopped within three days the dosage is increased to 60 grains (4 Gm.) daily. The drug is best given with milk and this will relieve much of the nausea attending its use.

More recently another derivative of sulfanilamide, namely sulfathiazole, has been added to our armamentarium. The original dosage used was 60 grains (4 Gm.) daily but recent work has led me to believe that in most cases 45 grains (3 Gm.) will be sufficient. This is given in divided doses by mouth and if it is at all nauseating its administration is likewise eased by giving it with milk. As previously mentioned, it has proved to be of inestimable value in the therapy of staphylococcic and gonococcic infections. In the latter conditions I believe that 60 grains (4 Gm.) daily is advisable and I have continued this for a period of from ten to fourteen days, although in all our cases the discharge was stopped and the urine was clear in from three to four days. Local treatment is instituted as previously described under the discussion concerning sulfapyridine.

TOXIC MANIFESTATIONS

When one surveys the many contributions to the literature with regard to the untoward reactions noticed following the administration of the sulfonamide compounds, the need for careful observation of each patient taking the drug becomes apparent. It is true that in the management of infections of the urinary tract these untoward reactions are less frequent than in the general field of therapy. Signs of toxicity may be due to sensitivity or idiosyncrasy to the medication. While the latter is more severe, it is less common. Sensitivity to the drug is more frequently noted to a greater or lesser degree and is almost always related to the dosage used and the total amount administered.

I have made it a practice never to administer any of the sulfonamide compounds unless the patient can be seen in from twenty-four to forty-eight hours. With this scheme I feel that we have been able to avert some of the more serious reactions frequently experienced. No doubt the main reason for the relative infrequency of the more serious toxic manifestations is the reduced dosage which has been found satisfactory in our field. Headache, malaise, vertigo, tinnitus, anorexia and nausea are frequently seen to a mild degree and usually will disappear on the third or fourth day the drug is taken. Patients with these mild to moderate symptoms should be observed closely, as these symptoms may be the precursors of more serious reactions. Cyanosis of a mild degree may be disregarded, but if it increases I

believe this is enough to warrant stopping the drug, as it may be an indication of an impending blood dyscrasia. It has been stated that sulfanilamide injures the blood-forming organs in from 4 to 5 per cent of cases. Hemolytic anemia of the acute and chronic form has been frequently reported, the acute form coming on within the first week of therapy and the chronic form not being seen for two or three weeks after treatment has begun. The development of granulocytopenia usually comes after the administration of large doses or prolonged treatment. It is a severe reaction and usually fatal. Unquestionably many of these blood conditions following administration of sulfanilamide could be avoided with more careful and frequent observation of patients. I am certain that a few extra blood counts when cyanosis is developing would often aid in averting these serious complications.

Dermatitis is a rather frequent complication and is of two types, the one localized to the exposed parts and the other a more general eruption over the entire surface of the body. The former type is caused by an increased sensitivity of the skin to light as a result of ingestion of the drug. The latter type is a toxic dermatitis. The presence of either form requires stopping the drug, but it can be resumed at a later date in the former type if the patient is instructed to keep out of the sunlight while taking the drug. With all the sulfonamide compounds I have found the dermatitis to be more likely to occur during the second course of the administration of these drugs, particularly if the second course of the drug is begun within eight days of the previous course. A certain sensitization must occur and the same fact has been noted by other observers. By prolonging the period between courses I feel that the frequency with which dermatitis occurs has been definitely reduced.

Sulfapyridine produces in general the same toxic disturbances as sulfanilamide but these are less severe with few exceptions. Nausea is more common but can frequently be relieved by taking the drug with milk. Gastric disturbances following the ingestion of sulfapyridine present but a small problem to the urologist as compared to the general physician because the former rarely needs to use large doses. A very important toxic sign is evidence of irritation along the urinary tract. As with sulfanilamide, an acetylated derivative of sulfapyridine is formed within the body and excreted in the urine. Crystals of this substance are frequently found in the urine of patients taking the drug and no doubt produce hematuria, either gross or microscopic, in approximately 5 per cent of cases. This complication is not important usually, but cases have been reported in which necropsy has shown complete casts of the calices, pelvis and ureters when large doses of the drug have been taken.

Azotulfamide and sulfanilyl-sulfanilamide produce similar toxic reactions to sulfanilamide itself but as a rule these side-effects are of a milder degree. Dimethyl-disulfanilamide and more recently sulfamethylthiazole, two drugs of generally lessened toxicity, have had to be discarded because of the frequency with which peripheral neuritis has appeared after their use. The same complication has occurred after sulfanilyl-sulfanilamide, only much less frequently.

For some months I have been using sulfathiazole and find it much less toxic than the parent substance. The usual symptoms seen after ingestion of sulfanilamide appear here also, but they are less severe. As yet I know of no disturbances simulating the nerve lesion

previously mentioned as following the administration of sulfamethylthiazole. Dermatitis does occur but again I have been able to decrease the incidence of this complication by prolonging the first course of the drug and waiting at least two weeks before again giving it in any dosage.

SUMMARY

Sulfanilamide and its related compounds have proved of inestimable value in the treatment of infections of the urinary tract.

In those cases in which the infection cannot be eradicated by chemotherapy, a thorough and complete search by a competent urologist should be advised because of the frequent association of complicating pathologic conditions such as stone, tumor, obstruction or cicatricial deformity.

A moderate sized dose is all that is needed in the treatment of most urologic infections.

The closest observation of patients taking these drugs is needed. The use of the sulfonamide compounds in the treatment of infection of the urinary tract is still in its early stages and true evaluation will necessitate continued experimental and clinical work in order to determine their efficacy in infections of certain types produced by the various organisms.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

McCURDY MODEL GAS MACHINE ACCEPTABLE

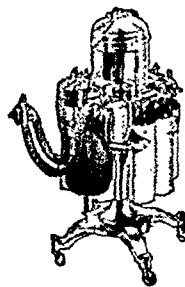
Manufacturer: Safety Gas Machine Company, Inc., 1163 Sedgwick Street, Chicago.

The McCurdy Model Gas Machine is designed for the administration of inhalation anesthesia, utilizing D cylinders of oxygen, carbon dioxide, nitrous oxide and ethylene with provision for an extra tank of each gas to be attached to the machine. An efficient reducing valve is connected with the yokes for each cylinder. Leaks from cylinder to cylinder cannot occur. The Augustana Model Gas Machine made by the same manufacturer, which is on the Council's list of accepted devices, is similar to the McCurdy Gas Machine.

Gases are admitted for delivery singly or in combination into a central mixing chamber through individual visible water manometer gages. The flow of each gas may be regulated by individual needle valves to obtain the desired proportion. The graduations on the manometers are apparently in gallons per hour.

A large lever on the top of the mixing chamber may be moved from the "on" to the "off" position if it is desired to by-pass the flowmeters for all gases. In the "on" position, needle valves on the top of the mixing chamber are used to regulate flow. In the "off" position, coarse flow valves on the base of the machine regulate the flow, without any registration of volume by the flowmeters. Apparently the latter provision is to enable the administrator to obtain the larger volumes necessary when using the apparatus for a semiclosed administration of gases, with the flutter valve in the circuit open to allow for exhalation.

A by-pass valve provides a quick source of oxygen. An ether vaporizer which is attached near the outflow from the machine permits the addition of varying percentages of ether to the gas mixture.



McCurdy Model Gas Machine.

The remainder of the apparatus consists of a so-called circle filter or a carbon dioxide absorption unit. The large canister in the circuit may be cut out at will, and an exhalation valve in the circuit may be kept closed for completely closed technic or opened for semiclosed technic.

The mask furnished with this machine is a transparent plastic type with rubber cushion for comfort and good fit. The breathing bag is of about 10 liters capacity. The whole apparatus rests on a substantial pedestal with rubber tired casters. A length of chain attached to the base trails on the floor, apparently for grounding purposes. The apparatus moves readily in spite of its weight.

The resistance to breathing is in the order of 3.5 cm. of water both on inspiration and on expiration, which is comparable to that found in most circle filters and is accounted for by the length of tubing and the inherent resistance to movement of the type of one-way valves incorporated. This resistance might be of some significance during anesthetization of a debilitated individual, especially during a long operation. It is doubtful whether any decrease in resistance could be obtained except by some radically different method of circulating gases.

Absorption of carbon dioxide is quite efficient, as shown by actual gas analysis; that is, compared to other circle filters and to and fro filters which we have tested. It must be recognized that no absorption units in use today reduce carbon dioxide to atmospheric levels.

The Council's clinical investigation revealed that in the hands of the skilled anesthetist the aforementioned gases and their combinations with ether may be efficiently administered with the McCurdy Model Gas Machine.

The Council voted to accept the McCurdy Model Gas Machine for inclusion on its list of accepted devices.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.
PAUL NICHOLAS LEECH, Secretary.

ORGANIC MERCURIAL COMPOUNDS AS BACTERICIDAL AGENTS

Although mercury, as simple and as complex compounds, has enjoyed popular use for the destruction of bacteria since the time of Koch, there is still no uniformity of opinion as to its true value. Whether this has arisen from lack of adequate controls or from misinterpretation of reported results, the fact remains that simple and complex mercury compounds still enjoy widespread popularity and enormous quantities are sold yearly.

In 1881 Koch reported that mercury bichloride was an effective agent in destroying the spores of even the most resistant bacteria, but in 1889 Geppert showed that the substance was poorly bactericidal but markedly bacteriostatic. In spite of the carefully controlled work of Geppert, mercury bichloride has remained in constant demand, and as each new mercurial is advanced for its antibacterial effects there is a renewed interest, often accompanied by an increasing false sense of security. In recent years solutions of mercurial compounds in which mercury has been combined with dye or other organic radicals have been advocated; because of their popularity they have largely replaced mercury bichloride, mercuric cyanide and mercuric iodide (or potassium mercuric iodide) for their reaction against infective agents; but even reports on these newer agents are not in harmony.

DEFINITION OF TERMS

No doubt one of the reasons for the existing confusion lies in the looseness with which such terms as "antiseptic," "sterilize," "germicide" and "bactericide" are used. According to an editorial which appeared in THE JOURNAL in 1927, a germicide is

defined in current medical textbooks as a "substance or agent that destroys micro-organisms so that they will not grow when placed in appropriate culture mediums"; an antiseptic is defined as a "substance that hinders or prevents the growth of micro-organisms but does not necessarily destroy their vitality."

As long ago as 1910 the Council on Pharmacy and Chemistry asserted that:

It seems of the greatest importance that antiseptic power be not mistaken for germicidal power and that physicians should be correctly informed as to these properties of disinfectants recommended to them, so that they may decide for themselves in every given case which action they wish to produce.

The term sterilization is often used, even by the physician, to connote germicidal or bactericidal or sometimes just bacteriostatic properties. In 1936 the Council formally went on record as "disapproving of the use of the terms 'sterile,' 'sterilize' and 'sterilization' in a bacteriologic sense other than in their correct scientific significance; i. e., meaning the absence or destruction of all micro-organisms." Many feel that they are "sterilizing" an instrument by immersing it for a definite period of time in some mercurial solution. Such an assumption is not necessarily valid, as no evidence has yet been offered¹ which is conclusive and accepted by all that there exists any mercurial compound which can be relied on to destroy the spores of anaerobic bacteria. Limitation exists even with nonsporulating bacteria.

About thirteen years ago the U. S. Bureau of Chemistry, which at that time was charged with the enforcement of the Food and Drug Act, came to the conclusion that the term "antiseptic," when used in the labeling of a medicinal product, was objectionable unless the preparation when used as directed would actually destroy micro-organisms. The Council on Pharmacy and Chemistry regards an antiseptic as having more disinfectant than germicidal properties and not to be necessarily highly germicidal.

In the Insecticide-Disinfectant Code² a disinfectant is defined as follows:

The term disinfectant as used herein means any chemical or drug or combination of chemicals or drugs intended to destroy one or more kinds of disease germs or other harmful micro-organisms (not including bacterial spores) when applied to all inanimate objects that might harbor disease germs.

EVALUATION BY THE PHENOL COEFFICIENT AND OTHER TESTS

Another factor which has been of little service in clarifying the picture is the use of the phenol coefficient test as a method of evaluating the antibacterial properties of the mercurials. Attention was drawn to this by the Council in a report of its 1939 annual meeting³ when the members cited the following paragraphs from circular 198 of the U. S. Department of Agriculture:

There are certain types of germicidal agents, such as many of the mercury compounds, which give very high results by phenol coefficient tests. Due to the high inhibitory value of such substances in preventing growth in the subcultures, these figures are frequently misleading. For germicides used in the disinfection of such objects as surgical instruments, this is of particular importance and must be taken into account. Failure to appreciate this characteristic of certain compounds is much more likely to lead to error when *Staphylococcus aureus* is used rather than *Eberthella typhi* as the test organism. That false values may not be obtained for products of this type, or for any other disinfectant giving suspiciously high results, the subcultures should contain very large amounts of medium or they should be retransferred by carrying at least four loopfuls from the first subculture to a second tube of broth, as recommended by Shippen.

Other groups of disinfectants in common use, for which the phenol coefficient method of testing is not well adapted, are those compounds containing chlorine as the active agent, as well as the oxidizing agents in general. These are affected so materially by the presence of organic matter that a phenol coefficient statement may grossly misrepresent their value under practical conditions of use and is very apt to be misleading to the consumer when placed on the label.

The Council pointed out that an unduly high and misleading phenol coefficient is given in the case of mercurial disinfectants because the retransfer method was omitted, and any bacteriologic

1. Brewer, J. H.: The Antibacterial Effects of Organic Mercurial Compounds, J. A. M. A. 112: 2009 (May 20) 1939.

2. Insecticide-Disinfectant Code, Soap 10: 81, 1934.

3. Annual Meeting of the Council on Pharmacy and Chemistry, J. A. M. A. 112: 2277 (June 3) 1939.

tests for mercurial compounds alleging bactericidal properties should be made under conditions of actual application to supplement a test under simplified and arbitrary conditions. For instance, it has been found that mercurials are rendered completely inert bacteriologically by the addition of relatively larger amounts of normal horse serum. To get a therapeutic result even in serum would require many times the lethal dose of the mercurial. This inactivation by serum has been studied quantitatively by Smith, Czarnetzky and Mudd.⁴ In view of such reports, the Council declared the phenol coefficient to be an inadequate basis for judging the antiseptic value of nonphenolic agents needing to be supplemented by tests under conditions of actual use.

The principle of the phenol coefficient test used in 1903 by Rideal and Walker is essentially that employed at present. The phenol coefficient is that figure which is obtained on dividing the greatest dilution of the disinfectant killing test organisms in a definite period of time by the greatest dilution of phenol killing in the same interval of time. There have been many attempts to improve on the original method but none have attained perfection. Knighton⁵ compared the Hygienic Laboratory method and the Food and Drug Administration phenol coefficient method with the Rideal and Walker method and demonstrated the variations in technic designed to simulate practical conditions. In addition, he reviewed other variations such as using different test organisms, adding sterilized fecal material and serum, wet and dry filter paper method, agar plate method and agar cup plate test. Not one has proved to be ideal.

Since the phenol coefficient test is of dependable value only for comparison of the efficiency of phenol and phenol-like compounds and does not take into account the destruction of bacterial spores or the part which organic material may play, various totally different procedures have been devised⁶ but little more success has been met, since in vitro experiments will not necessarily give the same experimental results in vivo or even when repeated in vitro.

Many tests are misleading because of misinterpretation of the results. According to Knighton,⁵ some of the faults are due to (a) comparing the usable dilution with the germicidal strength, (b) testing the material on only one or two types of organisms or, in the case of spore-forming bacteria, on the organisms in their vegetative form rather than on the spores, (c) failing to account for possible deterioration in volatile substances, (d) ignoring the fact that certain chemicals may behave differently when diluted or when combination occurs with other substances which are present, (e) confusion of terminology and (f) lack of appreciation, especially with the mercurial compounds, of the bacteriostatic substances giving exaggerated bactericidal value when the phenol coefficient test is used. Neutralization of the inhibiting factor by subculture, washing or a neutralizing agent must first be carried out to prevent false bactericidal values.

Thaysen⁷ criticized the British Standards Institution's technic of the Rideal-Walker test for the evaluation of antiseptics because of difficulties in obtaining consistent results which arise from the survival of a few of the bacteria when exposed to the solution to be tested. Transference of at least one cell to the growth tubes may be problematic on account of a too small number of surviving cells. To ensure transfer of the organisms would require transfer of much larger quantities of the solution than is required by the test. The British Standards Institution test requires an exposure of eight minutes, the Chick-Martin test an exposure of thirty minutes. However, the latter gives more consistent results than the Rideal-Walker test with a ten minute exposure. Complete destruction of *Bacterium typhosum* in phenol solutions requires one hour.

Apart from the lack of accurate tests for determining the true comparative bactericidal value of compounds in test tubes there remains the fact that any antibacterial effect observed in vitro will not necessarily be the same on living tissue. Factors here which will determine the eventual outcome include bactericidal action of normal blood, previous history of disease, type of organism, virulence, number of organisms present, presence of organic material and the tissue toxicity of the antibacterial agent. Because of the part played by phagocytosis in combating infection, Welch and Hunter⁸ made use of this phenomenon in developing a method of testing antiseptics by determining what they called a toxicity index, which is the highest dilution of antiseptic toxic for tissue (determined by the inhibition of phagocytosis) divided by the highest dilution capable of killing the test organism. This procedure is reminiscent of that performed by Salle and his associates,⁹ who determined a toxicity index by using chick embryo tissue. A summary of the tissue toxicity tests has been made by Knighton⁵ in an attempt to point out that there is a need for tests to determine any deleterious effect on the skin, as well as the relative efficiency of the substance tested.

Another factor which may influence the effectiveness of a germicide is the acidity. Bittenbender and his co-workers¹⁰ point out that acidity has been known since the time of Pasteur to affect the growth of some bacteria. Previous work¹¹ showed that a change in hydrogen ion concentration affected the action of some organic mercury compounds, phenolic compounds and other antibacterial agents. This work was confirmed by Bittenbender¹⁰ using *Staphylococcus aureus* and *Escherichia coli* as test organisms. The agents showed increased potency with an increase in the hydrogen ion concentration of the medium.

Rose and Miller¹² concur with the observations which suggest that test tube experiments give no true indication of the effectiveness of an antiseptic or germicide when applied to tissues or when mixed with blood, saliva and exudates. They studied certain mercurials in the presence of from 1 to 50 per cent blood solution with *Staphylococcus aureus* as the test organism and found that increase in blood concentration decreased antiseptic effectiveness by using the formula $C = Ke^{-mz}$, where C = concentration of blood (%), K = a constant for each antiseptic, e = base of naperian logarithms, m = coefficient of inactivation of the antiseptic and z = zone of inhibition of bacterial growth (mm.). It was concluded that the mercurials have no antiseptic action at certain critical blood levels. Hunt¹³ injected a strain of *Staphylococcus aureus* intravenously into mice and found that mercurial compounds failed to prevent infection or lessen necrosis if mixed with the bacterial suspension just before injection.

MODE OF ACTION

According to Brewer¹ the most generally accepted ideas regarding the manner in which the mercurials show antibacterial properties probably arise because mercury bichloride was known to coagulate the proteins by a direct combination with the tissues. It is now more or less believed that the mercurials precipitate bacterial protein. Modifications of this view, together with the surface absorption and enzyme destruction theories, have been reviewed by Brewer, but in conclusion he admits that not one of the suggested theories has offered a complete and satisfactory explanation.

8. Welch, Henry, and Hunter, A. C.: Method for Determining the Effect of Chemical Antiseptics on Phagocytosis, *Am. J. Public Health* 30: 129 (Feb.) 1940.

9. Salle, A. J.; McOmie, W. A.; Shechmeister, I. L., and Foord, D. C.: Evaluation of Group of Germicides by Tissue Culture Technic, *J. Bact.* 37: 639 (June) 1939.

10. Bittenbender, W. A.; Degering, E. F.; Tetrault, P. A.; Feasly, C. F., and Gwynn, B. H.: Bactericidal Properties of Commercial Antiseptics: A Further Study of the Effect of pH, *Indust. & Engin. Chem.* 32: 996 (July) 1940.

11. Goshorn, R. H.; Degering, E. F., and Tetrault, P. A.: Antiseptic and Bactericidal Action of Benzoic Acid and Inorganic Salts: Effect of pH, *Industrial & Engin. Chem.* 30: 646 (June) 1938.

12. Rose, S. B., and Miller, R. E.: Studies with the Agar Cup-Plate Medium: II. The Effect of Blood on Mercury Antiseptics, *Am. J. M. Sc.* 199: 338 (March) 1940.

13. Hunt, G. A.: Use of Cutaneous *Staphylococcus* Lesions in Mice for Evaluation of Germicidal Activity of Disinfectants, *J. Infect. Dis.* 60: 232 (March-April) 1937.

4. Smith, D. E.; Czarnetzky, E. J., and Mudd, Stuart: The Mechanism of Inactivation of Mercurial Antiseptics by Serum, and Its Implications Regarding the Possibility of Intravenous Antisepsis, *Am. J. M. Sc.* 192: 790 (Dec.) 1936.

5. Knighton, H. T.: Significance of Tests for Evaluation of Antiseptics and Germicides, *J. Am. Dent. A.* 26: 2047 (Dec.) 1939.

6. Peterson, J. B.: Mercurials: A Proposed Method of Laboratory Evaluation and Classification, *J. A. M. A.* 87: 223 (July 24) 1926.

7. Thaysen, A. C.: Some Observations on the Rideal-Walker Test, *J. Hyg.* 38: 558 (Sept.) 1938.

In 1917 Sollmann¹⁴ reported that it was difficult to kill bacteria on body surfaces because solutions which are definitely germicidal might destroy the tissues, and because chemical antiseptics are weakened by the presence of organic matter. If, however, it is possible to injure the bacteria in some manner, the injury may be enough to effect subsequent death of the bacteria either as a direct result of the cell injury or by aid of the tissue reactions.

Actual injury to the bacteria which have managed to get within the body tissues is even more difficult, since organic matter may be precipitated and hinder further any tissue penetration by the germicide that might conceivably occur.

COMPARATIVE VALUE

The efficiency of chemical disinfecting or germicidal agents is largely dependent on the form and material of objects to be sterilized. Attempted sterilization of utensils by chemical agents involves employment not only of solutions that are actually bactericidal but also of methods which ensure adequate contact between bacteria and solution. The latter is the more difficult part of the problem. Because the market is flooded with chemical agents which are as effective bacterially as or even better than a standard solution of phenol in ideal laboratory conditions, it does not necessarily follow that the same pathogenic organisms will be destroyed on instruments or skin which are protected by coatings of organic material whether it is dried mucus, coagulum or just grease and dirt.

Novak and Hall¹⁵ found an average of twelve staphylococci and diphtheroids per square centimeter on what was normally considered clean skin. Application of 50 per cent alcohol and 10 per cent acetone solution, a common solvent for antiseptics, destroyed 95 per cent of the bacteria on the skin. Only from 2 to 3 per cent more were killed when any commonly used skin antiseptic was added to this solvent. Tincture of green soap alone killed only 53 per cent of the skin bacteria. When skin antiseptics are desired, it is necessary to consider not only resident bacteria but also any transient bacteria that may be present. The same strains of an organism may show individual variation under different cultural environments.

Bass¹⁶ reviewed some of the previous literature and left open the suggestion that some of the antibacterial action attributed to the mercurials might be due to bacteriostasis. Using adult rabbits for experimentation with Birkhaug's method, which was reported in 1933, Bass tested a series of the more common agents. Using 70 per cent ethyl alcohol as a standard of comparison, which sterilized 27.7 per cent of skin areas treated, he found that sterilization of the skin by other agents ranged from 38 to 80 per cent. He found evidence that some of the newer organic preparations of mercury were of distinct value as antiseptics and possessed more germicidal activity than the older chlorides of mercury, but absolute sterilization was never obtained. Price¹⁷ has reported that 70 per cent by weight of ethyl alcohol is the most effective concentration of alcohol for antibacterial properties. Slight variations from this percentage lessens the bactericidal action. From his observations he evolved a simple technic for preoperative cleansing of the hands and arms. Essentially it consists of scrubbing the hands and arms with a brush, soap and warm water for seven minutes, drying them with a sterile towel, rinsing in 95 per cent alcohol to remove any remaining water, and then washing for three minutes in a basin well filled with 70 per cent alcohol (by weight). Later investigations by Price¹⁸ also revealed information on the germicidal values of mercury bichloride and of potassium mercuric iodide. When skin free of grease is washed in one of these mercurials there is formed a sterile impermeable "film" which protects the under-

lying cutaneous bacteria. This "film" is impervious to bacteria, slightly permeable to alcohol and very resistant to friction. However, beneath the "film" the bacteria are unharmed and multiply at a rapid rate. The formation of such a "film" probably explains why the older surgeons often enjoyed relative asepsis when operating without gloves. Price believes that mercury bichloride and potassium mercuric iodide (1:500) are of value in preoperative disinfection of the hands whenever an ungloved hand must be used in obstetrics or surgery. These agents may also have a place in the preparation of the field of operation but should not be depended on to effect sterilization at the site through which an incision is to be made.

Older forms of mercury, such as the bichloride, in addition to not killing spores on instruments, corrode the metal and may cause dermatitis when in prolonged contact with the skin. Because of their toxicity when injected parenterally, they could not be used in chemotherapy. About the close of the World War the first organic mercurials appeared with great claims for ability actually to sterilize instruments. However, these claims lacked support by way of adequate tests. Their inability to sterilize sutures was reported by Brewer,¹⁹ while making a survey for the Council on Pharmacy and Chemistry.

Examination by the Chemical Laboratory of the American Medical Association has revealed that decomposition with the liberation of free mercury of many organic mercurials occurs on standing. The preparations examined included solutions in ampules, lubricating jellies and creams. This work appears to indicate that the organic mercurials are not sufficiently stable to prevent partial disintegration from occurring over varying periods of time.

CONCLUSION

Mercurial preparations are used for antiseptic and disinfecting purposes, but they cannot be expected to destroy spores after several hours' exposure or even be relied on to destroy some nonsporulating bacteria. The organic compounds of mercury are claimed, in general, to be less irritating and less toxic than the older preparations of mercury, but their germicidal activity is in doubt in many instances, even though they may, and often do, have a highly bacteriostatic value. Because of their bacteriostatic ability the organic mercurials are of value as first aid prophylactic antiseptics and as preservatives of certain biologicals for parenteral use. Claims for their ability to penetrate deeply into living tissue and to act as chemotherapeutic agents have yet to be adequately supported.

Sterilization of contaminated instruments and dishes, whether by autoclaving, boiling water or live steam, is more simple, fairly rapid, inexpensive and more certain than by any chemical method known at the present time. Once the material is sterilized and kept dry in an airtight container, it will remain sterile for a considerable period.

It is thus apparent that the organic mercurials can be used for certain bacteriostatic purposes and in some instances for bactericidal effects. However, they cannot be expected to destroy pathogenic spores, and even their action on nonsporulating bacteria is limited. Skin sepsis is best prevented by a thorough cleansing with soap and water and a solvent such as alcohol and acetone before using any antiseptic agent. At present, ethyl alcohol (70 per cent by weight) appears to be one of the most reliable antibacterial agents.²⁰

No safe organic mercurial compound has yet been offered which will guarantee destruction of spores in suture material.

19. Brewer, J. H.: The Present Status of Sterility of Catgut Sutures on the American Market, *J. A. M. A.* **108**:722 (Feb. 27) 1937.

20. In practice, the amount of alcohol in a preparation is generally referred to in terms of per cent by volume. Certain regulations in pharmaceutical practice state that the per cent of alcohol always means "by volume," unless expressed in terms by weight. As ethyl alcohol U. S. P. varies somewhat in water content, generally from 94 to 95 per cent by volume, it is impossible to give a definite formula for preparing alcohol 70 per cent by weight. Probably the best method would be to add approximately 25 cc. of water to 100 cc. of alcohol and adjusting the mixture so that the specific gravity at a temperature of 25 °C. is 0.8658. A stock solution may be checked by determining the specific gravity. Alcoholometric tables appear in many books of analysis, and an official table appears in the U. S. P. XI. A Westphal balance, or a well graduated hydrometer, is satisfactory for determining specific gravity.

14. Sollmann, Torald: *The Actions of Drugs*, Philadelphia, W. B. Saunders Company, 1917.

15. Novak, Milan, and Hall, Harry: *Method for Determining Efficiency of Preoperative Skin Sterilization*, *Surgery* **5**:560 (April) 1939.

16. Bass, A. D.: An Experimental Comparison of Certain "Skin-Sterilizing" Agents, *J. Pharmacol. & Exper. Ther.* **66**:279 (July) 1939.

17. Price, P. B.: Ethyl Alcohol as a Germicide, *Arch. Surg.* **28**:528 (March) 1939.

18. Price, P. B.: Mercuric Chloride, Potassium Mercuric Iodide and Harrington's Solution in Skin Disinfection, *Surg., Gynec. & Obst.* **69**:594 (Nov.) 1939.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 14, 1940

AMERICAN COLLEGE OF SURGEONS JOINS FORCES WITH AMERICAN MEDICAL ASSOCIATION IN HOSPITAL CENSUS

Each year the Council on Medical Education and Hospitals of the American Medical Association takes a census of registered hospitals, numbering more than 6,000. The American College of Surgeons also has obtained statistical reports from hospitals already meeting the minimum standards of the College and those under consideration for approval. The combination of these reports into one simplified form will be welcome to the hospitals and especially to their administrative officers. Printed in triplicate, a single typing of the form supplies a report for each of the interested organizations and provides a carbon copy for the files of the hospital. All forms are coded for punch card tabulation. Thus, with a minimum of trouble and expense, both the College and the Council secure such information as is necessary for the continuance of their recognition. Also the compiled returns serve as a basis for the Hospital Number of *THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION*, which places essential information in the hands of all hospitals, physicians and others concerned. This should render unnecessary many of the questionnaires now sent to hospitals.

It is gratifying to record that the returns are coming in more promptly than in other years and that over 50 per cent of them were received within ten working days after mailing. Hospitals that have not yet responded should do so at once. Staff physicians can do a good turn by asking at the office whether the report has been completed and mailed.

The hospitals approved for the training of interns and residents will receive their questionnaires late in December so that the reports may cover the calendar year 1940.

The combined census is one feature of the program for increased cooperation between the American Medi-

cal Association and the American College of Surgeons. Another phase of this get-together movement is the coordination of hospital inspection so as to avoid duplication and extend inspection service for hospitals.

WAR MEDICINE—A NEW PUBLICATION

Beginning in January, the American Medical Association will publish a new periodical: "WAR MEDICINE," as a part of its contribution to the preparedness program. The editorial board of the publication will be the Committee on Information of the Division of Medical Sciences of the National Research Council. This committee includes Dr. Morris Fishbein, Editor of *THE JOURNAL*, as chairman, and the following associate editors: Mr. J. R. Bloomfield and Drs. John F. Fulton, Richard M. Hewitt, Ira V. Hiscock, Sanford V. Larkey and Robert N. Nye. In order to have direct cooperation with the governmental services, the following representatives of the Army and Navy Medical Corps and the United States Public Health Service have been chosen to cooperate with this editorial board: Col. C. C. Hillman, Com. Charles S. Stephenson and Dr. R. R. Spencer.

The Division of Medical Sciences of the National Research Council has developed a number of scientific committees which are actively at work preparing reports of various phases of medical service under military conditions. These official documents will be available to the new periodical for prompt publication. Already reports on chemotherapy, the standardization of the treatment of pneumonia, numerous problems concerned with medicine in aviation, peripheral nerve injuries, wound treatment, gas gangrene and similar subjects are being made available.

The American Medical Association, through its Committee on Medical Preparedness, is concerning itself with all the questions of personnel for preparedness and for military service. The official reports of this committee will also appear in the new periodical as well as special considerations that are given to economic and social problems of the medical profession in relationship to the emergency. Of especial importance also are the reports of official committees of the American Medical Association, such as the Council on Medical Education and Hospitals, the Council on Industrial Health and similar groups which will also be concerned with these problems.

Finally, much material is being developed by the Coordinating Committee on Medicine and Health of the Council of National Defense and by many other governmental agencies which are considering the national nutrition, the provision of hospital services and similar questions closely related to preparedness and defense.

The new publication will appear as a bimonthly. The Board of Trustees of the American Medical Association

tion, which has authorized its publication; has established a price of \$5 annually for the subscription. The periodical should be useful not only to the government services, which have indicated their wish to subscribe to this periodical for their official departments, but also to libraries and to individual physicians.

THE INDUSTRIAL NURSE

Competent industrial health service depends on the availability of physicians adequately trained in industrial medicine, hygiene and traumatic surgery. Ordinarily, however, assistance is necessary from other properly qualified professional personnel. Industrial medical departments provide excellent opportunities to nurses with proper aptitude, good comprehension of public health nursing methods and a sure sense of their own professional limitations. A clinical and administrative assistant of this character will be of immense aid to any industrial physician in the performance of many routine functions which make up the bulk of industrial dispensary procedure. The system works admirably under whole-time industrial physicians or under part-time physicians who spend regular visiting hours at a plant. In the absence of direct medical supervision, written standing orders, properly posted in the plant medical unit, will do much to inhibit assumption of services which require expert medical attention. Unfortunately, many of the smaller plants which have found it possible to arrange for some form of nursing service fail to recognize the need for such supervision or consider themselves unable to support even part-time medical aid. A nurse working under such conditions acts under heavy professional and ethical handicaps. Some form of medical supervisory arrangement is necessary to provide nurses with technical advice. The physicians on call for first aid and compensation work may be most helpful, particularly if they have some insight into the actual working environment. Committees on industrial health now being formed in county medical societies will find the industrial nursing field a fertile one for helpful and cooperative activity, both in a direct advisory capacity and as coordinators of private and public medical services. Frequently, they may be called to correct unhealthful industrial situations which the nurse uncovers. Unified service of this kind is already contemplated, using the part-time services of public health or visiting nurses paid for by small industry on a fee basis calculated according to hours per week required.

These relationships are particularly pertinent in view of the speeding up and intensification of industry that is occurring as part of the preparedness program. Many more nurses will be needed than are now available. They can make a valuable contribution to industry by supplying first aid and nursing care to plant personnel, assisting the physician in health examinations, and helping the worker to secure correction of defects through

reference to the family physician or other properly designated medical agency. The nurse is concerned with sanitary conditions within the plant and may in many ways promote the health and safety of industrial workers. The nurse should participate in the work of health education in industry and encourage sanitary and hygienic precautions that will diminish absenteeism due to illness and accident.

New requirements for industrial health service will demand much more trained personnel than is now available. Schools of nursing should concern themselves at once with courses in industrial hygiene not only to undergraduate but to graduate students. Better education regarding industrial hazards, industrial relationships and the principles of health organization will encourage industrialists to extend their employment of good industrial nursing services. The need for higher standards is well recognized by leaders in the nursing profession, and plans are currently under discussion for additional improvement. Community of interest is so great that no opportunity should be lost by the medical profession to assist the industrial nurse, individually and collectively, to elevate her professional status.

PROPOSED ADDITIONS TO AND DELETIONS FROM THE NEXT UNITED STATES PHARMACOPEIA

The new Revision Committee of the U. S. Pharmacopeia has already begun to consider recommendations on scope. A number of important policies were adopted at the 1940 U. S. Pharmacopeial Convention which apparently will be reflected in the type of articles to be included or deleted from the next revision. Because of the importance of the Pharmacopeia to the practice of medicine, the U. S. P. Subcommittee on Scope has wisely prepared a preliminary statement of the suggested changes. Both physicians and pharmacists should consider the proposals, and discussions may well be presented in the pharmaceutical and medical press. The president of the Pharmacopeial Convention and the chairman of the Subcommittee on Scope have outlined the policy under which medicinal substances have been admitted to the Pharmacopeia:

The Subcommittee on Scope, which decides admissions and deletions for a new Pharmacopeia, is primarily responsible for the value and usefulness of the book to the medical profession. The fundamental medical and pharmaceutical objectives of the Pharmacopeia from the time it was established have been to include a selected list of the best known and most thoroughly tested medicines of each revision period and also suitable usage or dosage forms or preparations of these important basic medicines. It has always been the aim of those responsible for the Pharmacopeia that it should be so comprehensive as to meet every need of medical practice, insofar as there are efficient medicinal products and medical aids known and available.

This principle of Pharmacopeial admissions has been maintained and practiced since 1820 and was emphatically reaffirmed by the Subcommittee on Scope during the recent meeting of the Committee of Revision. When it is determined that a medicinal substance or preparation fails to meet the standard of therapeutic excellence or service required by the Revision

Committee or when a patent situation intervenes, such a substance, or preparation, is denied admission to the Pharmacopeia. This policy of the Pharmacopeia of the United States is the basic policy for all pharmacopeias of the world. Under it is included any substance or preparation used in medicine which in the opinion of its experts is worthy of Pharmacopeial recognition. Under this accepted policy, the Pharmacopeia has been able to develop and maintain a unique voluntary service to medicine, pharmacy and the public, a contribution recognized and accepted by the medical and associated professions, and the manufacturing drug industry, and adopted by state and federal legislation.

Fifty-five additional products have been recommended for inclusion in the new Pharmacopeia, a few simply as pharmaceutical necessities. In addition, thirty or more substances have been recommended for inclusion, but because of trademark or patent involvements the names have been withheld until the committee has opportunity to give them further study and to discuss the question of proprietorship with the owners of the trademarks and patents. Elsewhere in this issue (see page 2110) may be found a list of additions and also a list containing titles of the products which the committee recommends to be deleted. The recommendations of the committee show constructive effort. On some items there may be a difference of opinion, particularly whether or not the products are sufficiently established to be recognized in the Pharmacopeia for purposes of use by the general practitioner.

Nomenclature of these products will be dealt with by another committee, which has indicated that, wherever possible, established nonproprietary terms will be used. The titles in themselves, as they appear in the present list, do not imply that the respective names are to be considered as final.

THE PROBLEM OF PSITTACOSIS

Psittacosis is primarily a disease of so-called psittacine birds such as parrots and parakeets. The disease is transmissible to man, however, and is characterized by high fever associated with symptoms of an atypical pneumonia. Occasionally the disease can be transmitted from man to man, but the most common source of human infection is from parrots and parakeets which have been kept as household pets. No doubt many infected birds will be distributed as Christmas presents, and the hazard at this time demands a warning.

Meyer and his colleagues¹ at the Hooper Foundation in San Francisco have been persistent in their research on this disease. Much information on the nature of the virus which causes psittacosis is now available. On the basis of ultrafiltration measurements verified by photomicrographic studies it has been determined that the infective particle of psittacosis has

a minimum size of from 0.2 to 0.3 micron. Furthermore the infective agent of psittacosis has been shown to be the elementary body itself and not a separable substance or an invisible particle of the same size. The virus can be satisfactorily cultivated on the chorio-allantoic membrane of the developing egg. Agglutinins for the elementary bodies of psittacosis have been produced experimentally in guinea pigs, and control experiments have proved that the agglutination reaction resulting was not due to the presence of foreign protein or virus contamination. Indeed, the virus of psittacosis as represented by the elementary bodies acts in all respects as a small micro-organism requiring an intracellular habitat for multiplication and survival. The particular value of the serologic investigations, however, resides in the fact that they have led to the demonstration that complement fixation tests with coccoid antigens prepared from virulent mouse spleens or Rivers-Li tissue cultures of the virus are specific in nature and serve as invaluable aids in the early and late diagnosis of human psittacosis. Preliminary observations indicate that either convalescent serum or a highly potent goat serum which has been produced may shorten the course of the human disease. A specific test is therefore available and new potentials for treatment are in sight.

Psittacosis is widely distributed among birds in this country. In one shipment of 161 parrots, parrotlets and conures from South America, Meyer and Eddy examined 158 following the preceding death of 3 of the birds. Both the Panama parrots and the macaws presented gross lesions of psittacosis in the form of emaciation and large spleens and livers with healed necroses. In fact, of the whole group only 15 parrotlets and 1 Wagner parrot were proved free of the virus of psittacosis. Similar high incidence of infection was found in shipments from Colombia and Australia.

Such high percentages of infection of imported birds for house pets underline the danger of wide distribution of human disease, and some effective means of eliminating the diseased birds is of great importance. One method employed has been to introduce the rice bird into new shipments of psittacine birds. This bird has been found susceptible to the virus and is ideal in certain respects for experiments. This exposure method, however, requires an observation period of not less than two to three months and might fail to answer the pertinent questions relative to latent psittacosis in the imported birds. In later experiments from 5 to 10 cc. of blood (depending on the size of the parrot) was withdrawn from the superficial ulnar vein without difficulty, provided the birds had been properly anesthetized with ether. The concentrated tissue culture in Rivers-Li medium was used in the preparation of antigens, and complement fixation reactions were performed according to a somewhat complex technique. These complement fixation reactions could be interpreted as indicative of previous contact of the parrots

1. Lazarus, A. S., and Meyer, K. F.: The Virus of Psittacosis, *J. Bact.* **38**: 121 (Aug.) 1939. Meyer, K. F., and Eddy, Bernice U.: Psittacosis in Importations of Psittacine Birds from the South American and Australian Continent, *J. Infect. Dis.* **65**: 234 (Nov.-Dec.) 1939; The Value of the Complement Fixation Test in the Diagnosis of Psittacosis, *ibid.* **65**: 225 (Nov.-Dec.) 1939.

with the psittacosis virus. There is little doubt, therefore, that the complement fixation test may prove valuable in detection of the presence of psittacosis in an importation and for separating the healthy from the recovered birds. Others² have confirmed the value of the test. The complement fixation test, besides its function in birds, has also proved its usefulness as a diagnostic aid in human psittacosis both early and late. Further laboratory investigations aimed at improvement and refinement of technics are indicated and the development of a more effective specific method of treating the disease in man. Most promising at present is the use of convalescent serum and goat serum.

THERAPEUTIC TRIALS WITH RADIO-ACTIVE PHOSPHORUS

Several radioactive substances with possibilities for medical application have been prepared with the use of the cyclotron. Up to now radioactive phosphorus has been tried therapeutically more than any other element. Phosphorus, artificially made radioactive, appears to be especially interesting because it is easily manufactured in the cyclotron, because its half-life is relatively long, 14.8 days, and because phosphorus is important in organic and inorganic metabolism generally. Its essential difference from natural inactive phosphorus, according to Lawrence and his co-workers,¹ resides in the fact that its nucleus contains an extra neutron and it emits beta rays (electrons) when administered in the form of sodium phosphate. Bone eventually would be expected to retain a larger percentage than any other tissue, and bone, with such a high phosphorus content, would get the greatest number of radioactive atoms per gram. From studies on leukemia in mice it was considered possible that the administration of large quantities of radiophosphorus would seem to offer a method of getting more or less selective radiation in this disease. With this basis, Lawrence and his colleagues carried out metabolic and clinical studies employing radiophosphorus in six cases of leukemia—one lymphatic, one monocytic and four myelogenous leukemia. Although the clinical results were doubtful, it appeared that decreases in the number of white blood cells occurred in a manner similar to that produced by roentgen irradiation when large doses of radiophosphorus were given to patients with leukemia.

A later report by Lawrence² describes five additional cases of chronic myelogenous or chronic lymphatic leukemia treated by the oral administration of radiophosphorus in the form of sodium phosphate with resultant responses similar to those usually following roentgen or radium therapy. Two additional cases of polycythe-

mia vera were also reported in which similar treatment resulted in a fall in the hemoglobin, red blood cell count and reticulocyte count without evident destruction of the red blood cells. The principal advantages of this treatment according to Lawrence are that it offers a means of giving the whole body radiation continuously over a period of two or more weeks in a single oral dose of sodium phosphate, and there are no irradiation reactions.

Warren's³ report on the treatment of leukemia by radioactive phosphorus—just published—involved the study of four cases of acute or subacute leukemia. Most of the radioactive phosphorus used in the treatment of these cases was obtained from the Harvard cyclotron and had a half-life of 14.5 days. The desired amount of radioactive phosphorus ranging from one to four millicurie equivalents was dissolved in 5 per cent dextrose and physiologic solution of sodium chloride prepared for intravenous use, sterilized and injected intravenously. The intravenous route of administration was adopted because of the disadvantage of the oral route in that the proportion absorbed by way of the gastrointestinal tract is variable, and frequently over 10 per cent may fail to be absorbed. Two patients showed no significant response beyond minor changes in white cell count, and both subsequently died. In the two others some clinical improvement was noted, as evidenced by the general condition, level of white cell count and condition of bone marrow.

As yet the use of radioactive phosphorus as a therapeutic method is in the preliminary stage: the results offer promise, but important factors remain to be elucidated, including the type and stage of leukemia which might be expected to respond and the dosage and route of administration, both of which are still on a purely arbitrary basis. No doubt further investigation will clarify these points so that radiophosphorus or some other radioactive element can become firmly established as an addition to therapeutic methods.

Current Comment

THE CLEVELAND SESSION

Already the Council on Scientific Assembly has met, local committees are being established, places of meeting have been organized and movement has begun toward the making of a successful session for the American Medical Association in Cleveland, June 2-6, 1941. Elsewhere in this issue appears a table listing the hotels in Cleveland, with the prices that have been established for various types of hotel accommodations. Recent sessions of the American Medical Association have been attended by many thousands of physicians; in fact more than 12,000 registered at the meeting in New York last year. Obviously, it is desirable for every physician who plans to attend the Cleveland ses-

2. Ruys, A. Charlotte; Noordam, A. L., and Vervoort, H.: Psittacosis in Amsterdam Detected with Aid of Complement Fixation Reaction, *Nederl. tijdschr. v. geneesk.* 83: 3776 (July 29) 1939.

1. Lawrence, J. H.; Scott, K. G., and Tuttle, L. W.: Studies on Leukemia with the Aid of Radioactive Phosphorus, *Internat. Clin.* 3: 33 (Sept.) 1939.

2. Lawrence, J. H.: Nuclear Physics and Therapy: Preliminary Report on a New Method for the Treatment of Leukemia and Polycythemia, *Radiology* 35: 51 (July) 1940.

3. Warren, Shields: The Treatment of Leukemia by Radioactive Phosphorus, *New England J. Med.* 223: 751 (Nov. 7) 1940.

sion to reserve space as soon as possible. The Hotel Committee in Cleveland is convinced that it will be able to accommodate satisfactorily all physicians who wish to attend, provided some inkling may be obtained soon of the number of physicians who will attend and the type of accommodations which they will require. The cooperation of the medical profession in this matter will insure a greater degree of comfort, a more successful convention and more general satisfaction than can be

secured in any other way. If you plan to go to Cleveland, write at once to Dr. Edward F. Kieger, Chairman of the Hotel Committee, Cleveland Convention & Visitors' Bureau, Inc., 1604 Terminal Tower, Cleveland, Ohio, using preferably the blank which appears on advertising page 36 in this issue. Indicate a first, second and third choice of hotel. Indicate whether or not you will require extra space for your wife, your children or any other guests who plan to accompany you.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

COUNCIL OF NATIONAL DEFENSE

Coordination of Health, Welfare and Related Defense Activities

Pursuant to the authority vested in it by section 2 of the Act of Aug. 29, 1916 (39 Stat. 649), the Council of National Defense, with the approval of the President, hereby designates the Federal Security Administrator as Coordinator of all health, medical, welfare, nutrition, recreation and other related fields of activity affecting the national defense. In the performance of this responsibility the Federal Security Administrator as Coordinator shall, in cooperation with the Advisory Commission to the Council of National Defense, formulate and execute plans, policies and programs designed to assure the provision of adequate services of this character to the nation during the national defense emergency; and to that end he shall coordinate the facilities of existing federal agencies with respect to these several fields of action and shall establish and maintain liaison with such other agencies, public or private, as he may deem necessary or desirable.

The Federal Security Administrator is authorized, with the approval of the President, to appoint such advisory committees and subcommittees with respect to health, medical, welfare, nutrition, recreation and related activities as he may find necessary or desirable to assist him in the performance of his coordinating duties. Such committees and subcommittees may include representatives from federal departments and agencies, state and local governments, organized private groups and the public at large. The members of advisory committees and subcommittees shall serve as such without compensation but shall be entitled to actual and necessary transportation, subsistence and other expenses incidental to the performance of their duties. Each committee and subcommittee shall operate under the direction and supervision of the Federal Security Administrator as Coordinator and shall serve at his pleasure.

The Health and Medical Committee established by order of the Council of National Defense, dated Sept. 19, 1940, is hereby transferred to the Federal Security Agency, and such committee shall hereafter exercise its duties and functions under the direction and supervision of the Federal Security Administrator. Vacan-

cies occurring in the membership of this committee shall hereafter be filled by appointment of the Federal Security Administrator, with the approval of the President. All rules and regulations, projects and activities of the committee required to be approved by the Council of National Defense or the President shall, prior to submission thereto, be approved by the Federal Security Administrator.

Within the limits of appropriations allocated for purposes encompassed by this order, the Federal Security Administrator may contract with and transfer funds to existing governmental agencies and institutions and may enter into contracts and agreements with individuals or educational or scientific institutions for studies, reports, experimental investigations and expert counsel.

HENRY L. STIMSON,
Secretary of War.
FRANK KNOX,
Secretary of the Navy.
HAROLD L. ICKES,
Secretary of the Interior.

CLAUDE R. WICKARD,
Secretary of Agriculture.
JESSE H. JONES,
Secretary of Commerce.
FRANCES PERKINS,
Secretary of Labor.

Approved:

FRANKLIN D. ROOSEVELT,
Nov. 28, 1940.

GENERAL CONFERENCE ON PSYCHIATRIC EXAMINATIONS

The Director of Selective Service, C. A. Dykstra, invited a number of leading specialists in the treatment of mental disorders to Washington, D. C., December 5, for a general conference on the standardization of psychiatric examinations of Selective Service trainees. On the program of the conference was a proposal to hold a series of conferences throughout the United States which would serve as "refresher" courses for the local board physicians who examine Selective Service registrants when they are called up for physical examination. Mr. Dykstra believes that if local board examining physicians and the specialists attached to medical advisory boards are given an opportunity to attend seminars on the subject it will tend to bring about a desired uniformity in the psychiatric examinations. Those who were invited to attend the conference in Washington, December 5, included Dr. Winfred Overholser, U. S. P. H. S., St. Elizabeth Hospital, Washington, D. C.;

Lieut. Col. William C. Porter, U. S. Army, Walter Reed Hospital, Washington, D. C.; Capt. Dallas G. Sutton, U. S. Navy, Naval Hospital, Washington D. C.; Dr. Howard W. Potter, Bellevue Hospital, New York; Dr. Harry A. Steckel, American Psychiatric Association, Syracuse, N. Y.; Dr. Martin J. Cooley, Veterans Administration, Washington, D. C.; Mr. Frederic Osborne, chief of Civilian Advisory Committee on Selective Service; Dr. Roscoe W. Hall, St. Elizabeth Hospital, Washington, D. C.; Dr. Harry Stack Sullivan, White Psychiatric Foundation, New York; Dr. Wendell S. Muncie, Johns Hopkins Hospital, Baltimore; Dr. Rose Chapman, Sheppard and Enoch Pratt Hospital, Towson, Md., and Lieut. Col. Charles B. Spruit, General Headquarters, Army War College.

STUDY OF AIRPLANE PILOTS

The assistant secretary of commerce, Robert H. Hinckley, has announced the completion of arrangements by which the Mayo Foundation will conduct extensive research into the correlation between physical examinations of civilian airplane pilots and their actual performance in flight. The Mayo Foundation will conduct this research as a public service and at its own expense, the only cost to the government being flight courses for several of the doctors conducting these studies. The aim will be to develop more accurate yardsticks to predict on the ground the relative ability of pilots and prospective pilots. Ten Mayo Foundation specialists in various fields who studied the student pilots on the ground followed them step by step through the flight courses. Several of the Mayo physicians are already flight surgeons and others will take the civilian pilot training courses along with the students who are studying.

CALIFORNIANS SEND SUPPLIES TO BRITISH RED CROSS

The Medical Committee of the British War Relief Association of Northern California has purchased several ambulances and mobile canteens and sent them to the British Red Cross; the committee has been sending also other medical and surgical supplies. A plan is under way now to purchase a desivac machine of 5 liters capacity, which prepares powdered blood plasma in which are all of the original vital blood elements except the erythrocytes and water. Powdered plasma will be sent to the British Red Cross, where the only preparation necessary to make it instantly available for intravenous transfusion will be the addition of sterile distilled water. Desivac machines for yielding powdered plasma are already in use in a few of the military hospitals in England. The committee considers that this machine will be a link also in the medical preparedness program of the United States if powdered plasma becomes necessary for our own military forces; it will also make powdered plasma available to public health departments in the San Francisco Bay area in case of a major industrial disaster.

The unit will be installed if feasible in a San Francisco teaching hospital and all its operations will be under direct supervision of doctors who have volunteered their services.

The machine will be purchased with donations; any one desiring to contribute for this purpose may send donations to the B. W. R. A., Northern California Plasma Fund, 100 Bush Street, San Francisco.

MEDICAL AND SURGICAL SUPPLY COMMITTEE

Nearly \$100,000 has been received by the Medical and Surgical Supply Committee of America, 420 Lexington Avenue, New York, in cash and medical supplies and equipment for shipment to emergency hospitals in England. The cash is converted into medical supplies. Among the contributors have been individuals and hospitals in various states and pharmaceutical houses, one of which contributed 1,000,000 vitamin capsules and tablets. The Anglo-American Committee for War Refugees cabled the committee requesting hot water bottles and rubber sheeting, and in response 500 hot water bottles and 1,000 yards of rubber sheeting are being shipped. The committee hopes to send a total of 1,000 first aid outfits and an equal number of operating sets to England before Christmas to help equip air raid shelters, first aid posts and auxiliary hospitals. According to Mrs. Ronald B. Balcom, executive chairman, the administrative expenses of the committee remain at less than 4.5 per cent of the contributions. New names on the National Committee are Drs. Chester D. Allen, William D. Anderson, Daniel H. Anthony, Julian B. Blue, Kinsey M. Buck, Edward G. Campbell, Willis C. Campbell, Arthur F. Cooper, Jewell M. Dorris, all of Memphis, Tenn.; Dr. Claude B. Squires of Charlotte, N. C., and Dr. Julian Deryl Hart of Durham, N. C., Dr. Thomas H. Cheavens of Dallas, Texas, and Dr. Joel J. Pressman of Los Angeles.

COMMITTEE ON NURSING APPOINTED

The Health and Medical Committee of the Council of National Defense announced membership of a subcommittee on nursing, of which Miss Mary Beard, director of nursing, American Red Cross, has been named chairman. Members are Miss Marion Howell, dean of the Frances Payne Bolton School of Nursing, Western Reserve University, Cleveland; Miss Nellie Hawkinson, professor of nursing education, University of Chicago; Sister M. Olivia, dean of the School of Nursing, Catholic University of America, Washington, D. C., and Miss Julia Stimson, chairman of nursing, Council of National Defense, and president of the American Nurses' Association, New York. Functions of the subcommittee on nursing are to conduct investigations and studies of the nursing needs of the nation and make recommendations for coordinating nursing requirements of the country as a whole with those for national defense.

NEW MILITARY HOSPITAL IN SANTA BARBARA

Plans have been announced for a new hospital in Santa Barbara, Calif., to cost approximately \$1,042,800 and with a capacity of 750 beds to be built in accordance with war department policy governing provision of such establishments for new stations. Full facilities will be provided for competent operation and administration and include such buildings as surgical, medical and isolation ward buildings, dental and eye, ear, nose and throat clinics, an infirmary for sick call and first aid, a complete laboratory, physical therapy building, administration and surgery buildings, mess halls, quarters for bachelor officers, for nurses and for other medical personnel, recreation buildings, post exchange, workshops and storage buildings, and buildings for the fire protection service. It is expected that the hospital will be ready for occupancy early in 1941.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

The following additional medical reserve corps officers had been ordered to extended active duty with the regular army by direction of the War Department, Washington, D. C., up to November 29:

CAMPBELL, Clayton C., Jr., 1st Lieut., Long Beach, Calif.
CAMPBELL, Paul Andrew, Captain, Chicago.
COOPER, Arlin Bernice, 1st Lieut., Ben Wheeler, Texas.
ESTES, Woodrow B., 1st Lieut., Miami, Fla.

EVANS, Wesley Mort, 1st Lieut., Munhall, Pa.
HEWLETT, Frank Wilson, 1st Lieut., Coral Gables, Fla.
HOLSCHER, Edward Charles, 1st Lieut., Kirkwood, Mo.
JAASTAD, Leonard Binning, 1st Lieut., Milwaukee.
LIPIN, Raymond Joseph, 1st Lieut., Pasadena, Md.
NOVAK, John Goodman, 1st Lieut., Pittsburgh.
RININGER, Harold Casper, Rockport, Ind.
SAWYER, Lester Jacob, 1st Lieut., San Francisco.
SHEAR, Manuel Heine, 1st Lieut., Austin, Texas.
WITTELS, Theodore S., 1st Lieut., Newton, Texas.

SECOND CORPS AREA

The following additional medical reserve corps officers had been ordered to active duty by the Commanding General, Second Corps Area, up to November 29. The Second Corps Area comprises the states of New York, New Jersey and Delaware.

AYER, Guy D., Jr., 1st Lieut., Cooperstown, N. Y.
BASTON, Frank K., 1st Lieut., Tulley, N. Y., 1st Military Area.
BLAUVELT, Willard J., 1st Lieut., Port Byron, N. Y., 1st Military Area.
BLEICHFELD, Samuel, Captain, 119 Highland Avenue, Buffalo, New York, 1st Military Area.
CALEF, Victor C., 1st Lieut., New York.
CARPENTER, Robert B., Captain, Buffalo.
DODGE, Lynn, Major, Fairport, N. Y.

FISHBEIN, Elliot, 1st Lieut., Paterson, N. J.
FREEMAN, Ray McArthur, Captain, Linden, N. J.
GERSHMAN, Maurice, 1st Lieut., Brooklyn, 2d Military Area.
HERO, Bryon A., 1st Lieut., Long Island City, N. Y., 2d Military Area.
KASICH, Milosh, Major, New York.
MARSH, Edward H., Major, 7 Leith Place, White Plains, New York, 2d Military Area.
MAXWELL, Cyrus H., Captain, Albany, N. Y.
MENDELSON, Michael, 1st Lieut., Binghamton, N. Y.
MORAN, John F., Jr., 1st Lieut., Lambertville, N. J.
PASCAL, Vincenzo, Lieut. Col., New York.
RAINEY, Harry G., 1st Lieut., Ogdensburg, N. Y., 1st Military Area.
RAPPOPORT, Milton, 1st Lieut., Brooklyn, 2d Military Area.
SMITH, Percy L., 1st Lieut., Dayton, N. J.
STANSBURY, Frederick C., 1st Lieut., Syracuse, N. Y.
WAUGH, David D., 1st Lieut., Brooklyn, 2d Military Area.
WINTER, Carl M., 1st Lieut., Camden, N. J., 3d Military Area.

THIRD CORPS AREA

Following is a list of additional medical reserve corps officers who up to November 29 had been ordered to extended active duty by Third Corps Area order. The Third Corps Area comprises the states of Pennsylvania, Virginia, District of Columbia and Maryland.

ABRAMOVITZ, Leonard Jerome, 1st Lieut., Baltimore.
BANKERT, Charles William, 1st Lieut., Linesville, Pa.
BASTACKY, Morris, 1st Lieut., Pittsburgh.
BIDUS, Leo Marion, 1st Lieut., Philadelphia.
BISHOP, William Russell, Captain, Flint Hill, Va.
BLUMBERG, Leon David, 1st Lieut., Philadelphia.
CARP, Albert Alexander, 1st Lieut., Philadelphia.
CHERKASKY, Martin, 1st Lieut., Philadelphia.
DEWOODY, Gerald McDowell, Captain, Center, Pa.
DROZD, Joseph, 1st Lieut., Baltimore.
ENGELMAN, Frank Ephraim, Captain, Pittsburgh.

GAEV, Samuel David, Captain, Philadelphia.
GRIFFITHS, John Owen, 1st Lieut., Philadelphia.
HABER, Richard Edward, 1st Lieut., Pittsburgh.
JOHNSON, William Arthur, 1st Lieut., Uniontown, Pa.
KRAUSZ, Martin Richard, 1st Lieut., Philadelphia.
LAWRY, Lee Llewellyn, Jr., 1st Lieut., Philadelphia.
LICHTENSTEIN, George Maurice, 1st Lieut., Philadelphia.
MERLIN, Albert Abraham, 1st Lieut., Philadelphia.
MICHAELSON, Ernest, 1st Lieut., Bladensburg, Md.
SACHS, Fred, 1st Lieut., Bloomsburg, Pa.
SCHWAB, John Edward, 1st Lieut., Philadelphia.
SISSON, Harold Edward, 1st Lieut., Haynesville, Va.
STANLEY, Thomas Zborowski, 1st Lieut., Wilkes-Barre, Pa.
STEINMETZ, Henry Gottlieb, Captain, Arlington, Va.
STRATTON, James David, 1st Lieut., Brackenridge, Pa.
VIOLETTI, Raffaele Lombardo, 1st Lieut., Philadelphia.
VOLKIN, Leonard Bernard, 1st Lieut., Ernest, Pa.
WARREN, Charles Weston, 1st Lieut., Upperville, Va.
WOODHOUSE, Samuel Lawrence, Jr., Captain, Philadelphia.

FOURTH CORPS AREA

The following additional medical reserve officers have been ordered to active duty by Fourth Corps Area Order since November 22. The Fourth Corps Area comprises the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana.

BELL, John A., Jr., 1st Lieut., Dublin, Ga.
BOWDEN, Ralph O., 1st Lieut., Savannah, Ga.
BRANDON, Robert W., Jr., 1st Lieut., Martin, Tenn.
BUMGARNER, John R., 1st Lieut., Wilkesboro, N. C.
CALDWELL, Gene D., 1st Lieut., Shreveport, La.
CATHELL, Edwin J., 1st Lieut., Lexington, N. C.
CHERRY, James H., 1st Lieut., Asheville, N. C.
CHEW, Nathaniel J., 1st Lieut., Bristol, Tenn.
CROOM, Robert D., Jr., Captain, 1st Lieut., Maxton, N. C.
CROW, Robert H., 1st Lieut., Cowpens, S. C.
DOWMAN, Charles E., 1st Lieut., Atlanta, Ga.
ELDRIDGE, Franklin G., Captain, Valdosta, Ga.
EVANS, Milton L., 1st Lieut., Memphis, Tenn.
FAILLA, Anthony, 1st Lieut., Pineville, La.
FERRELL, Thomas J., 1st Lieut., Waycross, Ga.
FINGER, Elliott, Captain, Marion, S. C.
FREEMAN, James V., 1st Lieut., Jacksonville, Fla.
GALIN, Albert N., 1st Lieut., Brunswick, Ga.
GOLSON, Willard R., Captain, Macon, Ga.
HAMILTON, Alfred T., 1st Lieut., Chapel Hill, N. C.
HAMMOND, Alfred F., Jr., 1st Lieut., Grifton, N. C.
HARPER, Sage, 1st Lieut., Wray, Ga.
HART, Oliver J., Captain, Winston-Salem, N. C.
HENSON, George C., Captain, Knoxville, Tenn.
HOCHFELDER, Bernard, 1st Lieut., New Orleans.
HOLDER, Franklin P., 1st Lieut., Eastman, Ga.
HOUSER, Frank M., 1st Lieut., Macon, Ga.
HUFSTEDLER, Fred E., 1st Lieut., Lenoir City, Tenn.

HUTCHINS, James D., 1st Lieut., Crystal Springs, Miss.
HYER, Yeaden M., 1st Lieut., Chester, S. C.
JONES, Lewis M., 1st Lieut., Opelika, Ala.
KENDALL, Cyrus E., 1st Lieut., Madison College, Tenn.
LESHNER, John H., 1st Lieut., Knoxville, Tenn.
LEWIS, Walter G., 1st Lieut., Stokesdale, N. C.
LYLES, Robin, 1st Lieut., Columbia, Tenn.
MACLENNAN, Edward R., 1st Lieut., Opp, Ala.
MANLEY, David B., 1st Lieut., Holopaw, Fla.
MILLER, James B., 1st Lieut., Columbia, Tenn.
MORROGH, Lailor A., Jr., 1st Lieut., Breaux Bridge, La.
NEVANS, Herman, 1st Lieut., Livingston, Tenn.
PERKINS, George E., 1st Lieut., Lake Worth, Fla.
POMERANCE, Joseph B., Captain, Miami Beach, Fla.
RAINEY, William T., Captain, Tiptonville, Tenn.
SAPPINGTON, Thomas A., 1st Lieut., Thomaston, Ga.
SINCLAIR, Robey T., Jr., 1st Lieut., Whiteville, N. C.
SLIPAKOFF, Leon, 1st Lieut., New Iberia, La.
SLOAN, William S., 1st Lieut., Wilson, N. C.
SMITH, Daniel L., Jr., 1st Lieut., Spartanburg, S. C.
SORRELLS, John E., 1st Lieut., Iowa, La.
STAPLETON, John L., 1st Lieut., Columbus, Ga.
TAYLOR, Harlan H., 1st Lieut., Cookeville, Tenn.
TIMMONS, Thaddeus A., 1st Lieut., Pamlico, S. C.
WALSH, John K., 1st Lieut., Florence, S. C.
WATT, Edward C., Jacksonville, Fla.
WHITFIELD, Robert L., Jr., Captain, Jamestown, Tenn.
WORK, Samuel D., Jr., 1st Lieut., Forsyth, Ga.
YOUNG, Henry D., Jr., 1st Lieut., Bushnell, Fla.

Orders Revoked

Orders have been revoked on the following named officers reported on a previous report:

ARP, Charles R., 1st Lieut., Atlanta, Ga.
BRABHAM, Vance W., Jr., 1st Lieut., Augusta, Ga.
HARRELL, Henry L., Captain, Ocala, Fla.

FIFTH CORPS AREA

The following additional medical reserve corps officers had been ordered by Fifth Corps Area Order to active duty up to November 22. The Fifth Corps Area comprises the states of Ohio, West Virginia, Indiana and Kentucky.

AIR, Clements W., 1st Lieut., Ludlow, Ky.
BATEMAN, Robert G., 1st Lieut., Richmond, Ky.
BLOUNT, Rankin C., 1st Lieut., Lexington, Ky.
BROSHEER, John R., 1st Lieut., Middlesboro, Ky.

COHEN, Robert, Captain, Louisville, Ky.
DITTMER, Jack E., 1st Lieut., Valparaiso, Ind.
FLAN, Moses, 1st Lieut., Paintsville, Ky.
HOLTZCLAW, Morris Richard, 1st Lieut., Somerset, Ky.
LOONEY, John E., 1st Lieut., Praise, Ky.
MCALLISTER, Max F., 1st Lieut., Outwood, Ky.
MCCOLLUM, Wendell D., 1st Lieut., Beattyville, Ky.
NOE, Joseph T., 1st Lieut., Wheelright, Ky.
PORTER, Robert F., 1st Lieut., Middlesboro, Ky.
STERNBERG, Elmer G., 1st Lieut., Cincinnati.
STINE, Frederick, 1st Lieut., Fort Thomas, Ky.

EIGHTH CORPS AREA

The following additional medical reserve officers had been ordered to active duty by Eighth Corps Area order up to December 6. The Eighth Corps Area comprises the states of Colorado, Arizona, New Mexico, Oklahoma and Texas.

AHERN, William Thomas Aloysius, 1st Lieut., Mesa Verde, Colo.
ALBI, Roger Vincent, 1st Lieut., Denver.
ANGUS, Howard, 1st Lieut., Lawton, Okla.
AUSTIN, Dale J., 1st Lieut., Dallas, Texas.
BERK, Ira Jay, Captain, McAllen, Texas.
BEST, Ralph L., 1st Lieut., Skiatook, Okla.
BLOSS, Claude M., 1st Lieut., Okemah, Okla.
BRALLIAR, John Seward, 1st Lieut., Wickenburg, Ariz.
BURNETT, Thomas Raynes, Major, Mission, Texas.
CARLOCK, John Hoyle, Jr., 1st Lieut., Ardmore, Okla.
CLARK, John Vincent, 1st Lieut., Oklahoma City.
CUNNINGHAM, Charles Donald, 1st Lieut., Seminole, Okla.
DIMOND, Edgar A., 1st Lieut., Muskogee, Okla.
EVANS, Robert Erle, 1st Lieut., Ada, Okla.
EWELL, William C., 1st Lieut., Tulsa, Okla.
FRY, Francis P., Jr., 1st Lieut., Frederick, Okla.
GALLAGHER, C. A., 1st Lieut., Oklahoma City.
GOOCH, James Oliver, 1st Lieut., Shamrock, Texas.
GRANT, Richard B., Jr., Captain, Bryan, Texas.
HANDLEY, James Jefferson, Major, Greenville, Texas.
HARTGRAVES, Thomas Anderson, Major, Phoenix, Ariz.
HAWKER, Laverne Joseph, 1st Lieut., Fort Worth, Texas.
HOLMES, Raynor E., Jr., 1st Lieut., Canon City, Colo.
HOPPER, John Jackson, 1st Lieut., Stanton, Texas.
HUGGINS, James Richard, 1st Lieut., Oklahoma City.
JORDAN, Robbie C., 1st Lieut., Austin, Texas.
KELLAM, Seth White, 1st Lieut., Menard, Texas.
KERNEK, Clyde, 1st Lieut., Holdenville, Okla.
KERNEK, Paul, 1st Lieut., Oklahoma City.
KUYKENDALL, Fred D., 1st Lieut., Eaton, Colo.
LEIGHT, Sidney B., 1st Lieut., Denver.
LEEMEE, Raymond Adolphe, 1st Lieut., Odessa, Texas.
LERNER, Ben Leonard, 1st Lieut., Houston, Texas.
LIVINGSTON, Lawrence G., Captain, Cordell, Okla.
McFARLING, James Everett, 1st Lieut., Humble, Texas.

MARTIN, Howard C., 1st Lieut., Oklahoma City.
MINOWITZ, David Louis, 1st Lieut., Fairplay, Colo.
NICKS, Frank Irvin, 1st Lieut., Manitou Springs, Colo.
O'NEILL, Francis Edward, 1st Lieut., Sanderson, Texas.
PEACOCK, George Eugene, 1st Lieut., Jacksonville, Texas.
PHILLIPS, Oliver Mack, 1st Lieut., Fort Worth, Texas.
PICKETT, Britton E., Jr., 1st Lieut., Carrizo Springs, Texas.
PIERSON, Marcus A., 1st Lieut., Galveston, Texas.
RAFTER, John Ralph, 1st Lieut., Muskogee, Okla.
RECORDS, John Williams, 1st Lieut., Oklahoma City.
ROARK, Frank Earl, 1st Lieut., Monticello, Utah.
SANGER, Paul G., 1st Lieut., Vinita, Okla.
SCHUESSLER, Willard W., Captain, Dallas, Texas.
SEYLER, Louis Walter, 1st Lieut., Commerce, Texas.
SIEVER, James Monroe, 1st Lieut., Dallas, Texas.
SIMON, John Franklin, 1st Lieut., Alva, Okla.
STUBBS, James B., 1st Lieut., Sweetwater, Texas.
STUMP, Robert M., Captain, Phoenix, Ariz.
SWANSON, Howard Edward, 1st Lieut., Denver.
SWEARINGEN, Robert Goodwin, Captain, Corpus Christi, Texas.
SWINNY, Boen, Major, San Antonio, Texas.
SWITZER, Fred D., 1st Lieut., Hugo, Okla.
TUBBS, William M., 1st Lieut., Silver City, N. M.
TURNBOW, William Ray, 1st Lieut., Tulsa, Okla.
VAUGHAN, Luther Matthews, 1st Lieut., Houston, Texas.
WAGNER, Gerald W., 1st Lieut., McKinney, Texas.
WILKERSON, John M., 1st Lieut., Checotah, Okla.
WILSON, Jewell R., 1st Lieut., Seminole, Okla.
ZEDLER, Garland Gus, 1st Lieut., Austin, Texas.
ZEHNPFENNIG, Urban H., 1st Lieut., Merkel, Texas.

Orders Revoked

The recent Eighth Corps Area headquarters order assigning the following medical reserve corps officers to active duty have been revoked:

COOPER, Elmer E., 1st Lieut., Nogales, Ariz.
MARTIN, Howard C., 1st Lieut., Oklahoma City.
ROARK, Frank Earl, 1st Lieut., Monticello, Utah.
STOUGH, Austin R., 1st Lieut., McAlester, Okla.
WALLACE, Gordon K., Captain, Dallas, Texas.

NAVAL RESERVE OFFICERS ORDERED TO ACTIVE DUTY

The following additional naval reserve officers have been ordered to active duty:

ASHTON, Wilbur L., Lieut. Comdr., M. C.-V. (S), Umatillo, Fla., Naval Air Station, Jacksonville, Fla.
BENJAMIN, Emanuel W., Lieut. Comdr., M. C.-V. (S), Providence, R. I., Naval Hospital, Newport, R. I.
BOLES, Albert, Lieut. Comdr., M. C.-O., Oakland, Calif., Naval Air Station, Alameda, Calif.
CARTER, Curtis H., Lieut. (j. g.) M. C.-V. (G), Augusta, Ga., Naval Hospital, Pensacola, Fla.
CHAMBERLAIN, John W., Lieut. (j. g.) M. C.-O., Belmont, Mass., Naval Reserve Aviation Base, Squantum, Mass.
FRANCE, Richard, Lieut., M. C.-V. (S), Baltimore, Naval Hospital, Philadelphia.
GEIBEL, Frank B. C., Lieut., M. C.-V. (S), Washington, D. C., Naval Hospital, Philadelphia.
GROVE, Pembroke, T., Lieut. (j. g.) M. C.-V. (S), Washington, D. C., Naval Hospital, San Diego, Calif.
HALBACH, Robert M., Lieut. Comdr., M. C.-V. (S), Jamestown, R. I., Naval Hospital, Newport, R. I.
HANSON, Frederick C., Lieut., M. C.-V. (S), Providence, R. I., Naval Torpedo Station, Newport, R. I.
HORWITZ, Ellis Rerry, Lieut. Comdr., M. C.-V. (S), Philadelphia, Naval Hospital, Philadelphia.
HUBER, Paul R., Lieut. Comdr., M. C.-O., Chicago, Ninth Naval District Headquarters, Great Lakes, Ill.
HUGHES, William N., Lieut. Comdr., M. C.-V. (S), Providence, R. I., Naval Hospital, Newport, R. I.
IVORY, Harry S., Lieut. Comdr., M. C.-V. (S), Point Pleasant, N. J., Naval Air Station, Lakehurst, N. J.

KEARNS, Jerry J., Lieut. Comdr., M. C.-V. (S), Chicago, Naval Training Station, Great Lakes, Ill.
LLOYD, Allen S., Lieut., M. C.-V. (S), Los Angeles, Norfolk Naval Hospital, Portsmouth, Va.
LUPTON, Charles H., Lieut. Comdr., M. C.-V. (S), Norfolk, Va., Norfolk Naval Hospital, Portsmouth, Va.
MACALUSO, Anthony, Lieut. Comdr., M. C.-O., Newton, Mass., Naval Reserve Aviation Base, Squantum, Mass.
NORTHINGTON, Page O., Comdr., M. C.-O., New York, Third Naval District Headquarters, New York.
O'CONNOR, Harry A. D., Lieut. Comdr., M. C.-V. (S), New York, Naval Hospital, Brooklyn.
PAGE, Henry F., Lieut. (j. g.) M. C.-V. (S), Philadelphia, Naval Hospital, Philadelphia.
SCARNEY, Herman D., Lieut., M. C.-O., Detroit, Naval Reserve Aviation Base, Detroit (Grosse Ile), Mich.
SCHMIDHOFFER, Ernst, Lieut. (j. g.) M. C.-V. (S), Boston, Naval Hospital, Chelsea, Mass.
SCHNEIDER, Herbert H., Lieut. (j. g.) M. C.-V. (G), Rochester, Minn., Naval Hospital, Pensacola, Fla.
SCHWAB, William John, Lieut. (j. g.) M. C.-V. (G), Providence, R. I., Naval Torpedo Station, Newport, R. I.
SMART, Frank P., Lieut. Comdr., M. C.-V. (S), Norfolk, Va., Norfolk Naval Hospital, Portsmouth, Va.
STEINMUELLER, Karl J., Lieut. Comdr., M. C.-V. (S), Baltimore, Naval Hospital, Annapolis, Md.
TURNER, Howard K., Lieut. Comdr., M. C.-V. (S), Providence, R. I., Naval Hospital, Newport, R. I.
WEAVER, Harry S., Jr., Lieut., M. C.-O., Philadelphia, Fourth Naval District Headquarters, Philadelphia.
WITTON, Cecil L., Lieut., M. C.-V. (S), Central Islip, N. Y., Naval Training Station, Newport, R. I.

ORGANIZATION SECTION

ASSOCIATED HEALTH FOUNDATION, INC.

The Associated Health Foundation, Inc., with offices at 57 West Fifty-Seventh Street, New York, has received a license from the State Department of Insurance as provided under the recent amendment to the New York state insurance laws and has been approved by the State Department of Social Welfare. The foundation is not directly connected with or controlled by either the Medical Society of the State of New York or any county medical society. It is a nonprofit, medical expense indemnity plan organized in accordance with the law referred to. It is managed by a nonsalaried board of trustees made up of fifteen physicians and ten laymen. Medical matters are handled by a medical board composed of eight physicians. Any physician licensed in the state of New York is eligible to become a participating member of the plan. Members are permitted free choice of any physician who agrees to the terms of the plan.

The plan is designed to provide adequate medical care for persons below the "comfort level." Annual income limits are from \$1,800 for a single person to \$3,000 for a family with two or more children. Subscribers' dues are \$18 a year for a single person, \$30 a year for husband and wife, \$12 a year for a dependent child between 16 and 18 years old and \$7.50 for a dependent child under 16 years of age. For this the subscriber receives "complete medical and surgical care, including x-ray and laboratory tests from the underwriting physicians." The following classes of cases are excluded: workmen's compensation, elective surgery during the first eleven months, obstetric care during the first ten months, drug addiction, chronic alcoholic conditions, venereal diseases and nervous and

mental diseases. Services are also not given to any one who "prior to or at the time of their application for membership" have had any one of the following diseases: insanity, pernicious anemia, cancer, diabetes, psoriasis or any incurable skin disease, tuberculosis, chronic nephritis, osteomyelitis or chronic heart disease, or for any disease or condition existing at the time of the subscriber's application, venereal diseases during the first ten months, and plastic or cosmetic surgery.

The incomes from subscribers are to be divided as follows: 20 per cent for administration, and of the remaining 80 per cent "60 per cent thereof is used to pay general practitioners on a capitation basis and the remaining 40 per cent to pay specialists, consultants, surgeons, x-ray and laboratory men on a unit basis using the schedule of fees payable for services rendered under the workmen's compensation schedule as a basis." This scheme of distribution applied to the \$18 annual fee for an individual would give \$3.60 for administration, \$8.64 for the capitation fee for general practitioners and \$5.70 for consultants, x-ray and laboratory service. The amount available per person for physicians on the family rate would be still less. A physician who enters into this agreement can terminate his participation only after giving the corporation notice in writing "and such termination shall not be effective until thirteen months from the date of such notice." There is no deductible clause or limit to the amount of services which may be demanded and given during a contract year. The physician is to be paid, as explained, approximately 48 per cent of the subscriber's premiums regardless of the amount of service the physician gives to the subscriber.

OFFICIAL NOTES

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the A. M. A. meeting at Cleveland on June 3, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the programs, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and broadcast it at another hour or even on another day. It is advisable therefore to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in *THE JOURNAL* and monthly in *Hygeia*, the Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 18.	A Stitch in Time.
December 25.	The Country Doctor.
January 1.	Otorhinolaryngologist.

THE CLEVELAND SESSION

Applications for Hotel Reservations

A list of Cleveland hotels together with the rates for rooms may be found on advertising page 36 of this issue of *THE JOURNAL*. With this list will be found an application form that may be used to secure reservations through the Subcommittee on Hotels of the Local Committee on Arrangements. This application form may be clipped and, when it is properly filled in, should be sent at once to Dr. Edward F. Kieger, Chairman of the Subcommittee on Hotels, Cleveland Convention and Visitors' Bureau, Inc., 1604 Terminal Tower, Cleveland, Ohio.

Those who expect to attend the annual session of the American Medical Association should send in their applications at the earliest possible time. Applicants for reservations are especially requested to include a second and a third choice in order that good accommodations may be assured if the desired reservation cannot be had at the hotel of preference. It will greatly expedite matters if requests for reservations are addressed directly to Dr. Kieger.

Motion Pictures in the Scientific Exhibit

The Committee on Scientific Exhibit announces that motion pictures in the Scientific Exhibit at the Cleveland session will be shown in areas provided for that purpose rather than in exhibit booths. Application blanks for a place on the motion picture program may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Regional Meeting.—The Northeastern Division of the Medical Association of the State of Alabama met at Alexander City, October 10, with the Tallapoosa County Medical Society acting as host. The program included:

Dr. Henry Ernest Askin, Alexander City, Convulsions.
Dr. James R. Garber, Birmingham, Diagnosis in Obstetrics.
Dr. Amos C. Gipson, Gadsden, The Role of Allergy in Pediatric Practice.
Dr. James O. Morgan, Gadsden, Indications for Surgery in Peptic Ulcer.
Dr. George Knox Spearman, Anniston, Perennial Hay Fever.
Dr. James Marvin Washam, Talladega, Appendicitis.

ARKANSAS

District Meetings.—Dr. Augustus A. Street, Vicksburg, Miss., discussed "Duodenal Ulcer" before the Fifth Councilor District Medical Society in Camden, October 10, and Dr. William H. Anderson, Booneville, president of the Mississippi State Medical Association, "A Doctor's Duty to Himself, to His Fellow Men and to the Public."—The Second District Medical Society met in Batesville, October 14. Drs. William T. Pride, Memphis, Tenn., discussed "Some of the Common Difficulties in Obstetrics" and Darmon A. Rhinehart, Little Rock, "X-Ray Treatment for Menorrhagia."—The Third Councilor District Medical Society was addressed in Helena, October 24, by Drs. Robert Lyle Motley, Memphis, Tenn., on "Indication and Uses of Sulfanilamide, Sulfapyridine, Sulfathiazole"; David T. Hyatt, Little Rock, "Vitamin Therapy"; Alan G. Cazort, Little Rock, "Allergic Dermatitis," and William R. Brooksher, Little Rock, "Medical Preparedness." The dinner session was addressed by Dr. Downey L. Harris, St. Louis, on "Rabies."

CALIFORNIA

State Board of Examiners.—Dr. Hugo M. Kersten, Los Angeles, has been appointed a member of the state board of medical examiners, succeeding Dr. William R. Molony Sr., Los Angeles, whose term expired last January. Dr. Charles B. Pinkham, San Francisco, was reappointed.

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in California is required by law to register annually, on or before January 1, with the secretary-treasurer of the board of medical examiners and at that time to pay a fee of \$2. Failure to pay the required fee within sixty days after January 1 works a revocation of a license, and thereafter a license may be reissued only after application and the payment of a \$10 penalty.

CONNECTICUT

Personal.—Dr. Hazen A. Calhoun Jr., Middletown, has been appointed health officer of Haddam, succeeding Dr. Noah A. Burr.—Dr. William F. Verdi, New Haven, has received the gold medal award of the New Haven Advertising Club for his "outstanding contributions to the community."

Annual Registration Due During January.—Every practitioner of medicine and surgery holding a license to practice in Connecticut is required by law to register during January with the state department of health and at that time to pay a fee of \$2. Licentiates who have retired from active practice or who live out of the state must register annually but need not pay a fee. A practitioner failing to register is liable to a fine of not more than \$5.

Society News.—The Association of Connecticut Tumor Clinics was addressed in Bridgeport, October 17, among others, by Drs. Berkley M. Parmelee on "Irradiation Therapy for Cancer of the Breast" and William L. Weadon, "Treatment of Local Recurrences and Metastases."—Francis John Worsley Roughton, Ph.D., lecturer on physicochemical aspects of physiology, University of Cambridge, England, lectured at a special meeting of the Yale Medical Society, November 19, in New Haven, on "Recent Work on the Chemistry and Functions of Carbonic Anhydrase."

DISTRICT OF COLUMBIA

Changes in Faculty.—Dr. Edward J. Cummings, associate professor of clinical ophthalmology, has been promoted to professor at Georgetown University School of Medicine, Washington, newspapers announce. Other promotions include Dr. William McC. Ballinger to associate professor of gastroenterology and Dr. Edgar W. Davis to professor of clinical surgery.

Course in Aviation Medicine.—The second annual post-graduate course in aviation medicine, including aviation ophthalmology, for graduates in medicine will be held at George Washington University School of Medicine, Washington, D. C., February 3-7. Nineteen guests will lecture on the following subjects, among others:

Physiologic Problems Incident to Flying.
Motility of the Eye.
Color Vision and Night Blindness.
Stereopsis and Depth Perception.
Fundus of the Eye.
Refraction.
Aniseikonia as It Relates to Aviation.
Otolaryngology in Relation to Aviation.
Effect of Altitude in Relation to Military Flying.
Interpretations of Neurologic Signs in Aviation.
Methods of Administration of Oxygen During Flights at High Altitudes.

FLORIDA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Florida is required by law to register annually, on or before January 1, with the secretary of the state board of health and at that time to pay a fee of \$1. A licentiate failing to register annually is liable to a fine of not more than \$50.

GEORGIA

Dr. Lahey to Give Memorial Lecture.—Dr. Frank H. Lahey, Boston, President-Elect of the American Medical Association, will deliver the second Floyd Wilcox McRae Memorial Lecture, December 16, before the Fulton County Medical Society, Atlanta. His subject will be "The Management of Gastric, Duodenal and Jejunal Lesions."

University News.—A sum of \$100,000 has been presented to the University of Georgia by S. Price Gilbert, former associate justice of the Georgia supreme court, to construct an infirmary building. According to the *New York Times*, the infirmary will be named in honor of Justice Gilbert's father, the late Dr. Jasper Newton Gilbert, who served with the medical corps of the Confederate Army in the Civil War and later was a country doctor in Georgia. Dr. Gilbert, who lived in Columbus, was graduated at the Medical College of Georgia, Augusta, in 1855.

ILLINOIS

Research Fellowships in Medicine and Dentistry.—The Graduate School of the University of Illinois has established four research fellowships to be awarded for one year in the fields of medicine and dentistry in Chicago at a stipend of \$1,200 a year (calendar year with one month's vacation). Fellows are eligible for reappointment in competition with the new applicants. Candidates for these fellowships must have completed a training of not less than eight years beyond high school graduation. This training may have been acquired in any one of the following ways, or the equivalent thereof:

1. Work leading to the B.S. and M.D. degrees (in some instances the candidates would have the M.D. degree, or an additional year or two of hospital training beyond the intern year).
2. Work leading to the B.S., M.S. and D.D.S. degrees.
3. Work leading to the B.S. or B.A. degree in a four year collegiate course and to the D.D.S. degree.
4. Work leading to the B.S., D.D.S. and M.D. degrees.

Candidates should indicate the field of research in which they are interested and submit complete transcripts of their scholastic credits, together with the names of three former science teachers as references. March 1 is the deadline for acceptance of applications. Announcement of the fellowship awards will be made April 1, becoming effective September 1. Formal application blanks may be secured from the Secretary of the Committee on Graduate Work in Medicine and Dentistry, 1853 West Polk Street, Chicago.

IOWA

Society News.—The Des Moines Academy of Medicine and the Polk County Medical Society was addressed, November 20, by Drs. James Barrett Brown, St. Louis, on "Traumatic Surgery" and Andrew C. Ivy, Chicago, "Relation of Physiology to Modern Medicine."

Personal.—Dr. Eric P. Pfeiffer, formerly of Oakville, has been appointed director of the vital statistics division of the state department of health, effective October 1.—Dr. Lester A. Royal, West Liberty, has been named governor of district 132 of Rotary International.

The Rockwood Lecture.—Dr. Isaac Starr, Milton Bixler Hartzell research professor of therapeutics, University of Pennsylvania School of Medicine, Philadelphia, gave the fourth annual Paul Reed Rockwood Lecture of the State University of Iowa College of Medicine in Iowa City, November 13. His subject was "The Ballistocardiogram; Its Contribution to Our Knowledge of the Commoner Diseases Affecting the Heart and Circulation."

LOUISIANA

Annual Renewal Due January 1.—Every practitioner of medicine and surgery holding a certificate to practice in Louisiana is required by law to have his certificate renewed annually, on or before January 1, by the secretary-treasurer of the state board of medical examiners and at that time to pay a fee of \$2. The board may by unanimous vote revoke any certificate not renewed.

Society News.—The meeting of the Louisiana Association of Pathologists, November 25, in New Orleans, was opened with an address by Dr. Edwin H. Lawson. Other speakers were Drs. Bjarne Pearson on "Carcinoma of the Cervix Uteri, Its Effect on the Urinary Tract"; Albert E. Casey, "Mitosis Counts in Neoplasia," and Joseph B. Pasternack, "Methods for Rapid Preparation of Paraffin Sections."—Among other speakers, Arthur O. Kastler, Ph.D., Drs. Samuel B. Nadler and Michael E. DeBakey presented a symposium on the recent advances in vitamins before the Orleans Parish Medical Society, November 11. A special scientific session was held with the U. S. Marine Hospital staff, November 22. Dr. John A. Trautman talked on "Sulfonamides in the Treatment of Gonorrhea in the Male" and Dr. William L. Smith presented a case report on a typhoid carrier.

MINNESOTA

Annual Registration Due During January.—Every practitioner of medicine and surgery holding a license to practice in Minnesota is required by law to register annually during January with the secretary of the board of medical examiners and at that time to pay a fee of \$2. A licentiate who practices without renewing his license is guilty of a misdemeanor and is liable to prosecution.

Tuberculosis Survey.—The Minnesota State Medical Association has selected Meeker County as the first county in which a statewide campaign to free Minnesota from tuberculosis will be launched. The plan calls for extending to adults through family groups the same preventive service now given to children in the public schools, using the Mantoux test. The project will be under the direction of the committee on tuberculosis of the state medical association, of which Dr. J. Arthur Myers, Minneapolis, is chairman. Cooperating agencies include the Minnesota Public Health Association, the bureau of tuberculosis of the state division of social welfare, the Meeker-Kandiyohi-Swift Counties Medical Society, the Meeker County Christmas Seal Committee and the state department of health.

Society News.—The Ramsey County Medical Society was addressed, November 25, by Drs. Emmett V. Kenefick, St. Paul, on "Leukemias and Leukemoid Reactions"; Alexander E. Brown, Rochester, "Recent Advances in Therapy by Sulfanilamide and Its Related Compounds," and Gordon R. Kamman, St. Paul, "The Rorschach Test as a Method of Personality Analysis."—The general staff of the Mayo Clinic met with the Olmsted-Houston-Fillmore-Dodge Counties Medical Society, November 6; the program was devoted to a symposium on first aid by the physician casually present at an accident. The speakers were Drs. John S. Lundy, John W. Pender, Edward B. Tuohy, Alfred W. Adson, Robert D. Mussey, Gordon B. New and Albert J. Lobb, LL.B., all of Rochester.

MISSOURI

Pilgrimage to Beaumont's Grave.—The annual birthday pilgrimage to William Beaumont's grave, sponsored by the St. Louis Medical Society, was held November 21. Alphonse M. Schwitalla, S.J., made the principal address; Mayor Bernard F. Dickmann placed a wreath on the grave for the city of St. Louis; Dr. Cyrus E. Burford, president of the state medical association, also placed a wreath, and Dr. Herbert S. Langsdorf as president represented the St. Louis City Medical Society.

NEW JERSEY

Interim Meeting of House of Delegates.—The first interim meeting of the house of delegates of the Medical Society of New Jersey was held in Newark, November 28. The following progress reports were presented: medical service administration, by Dr. Elton W. Lance, Rahway, president of the board of governors; medical preparedness committee, by Dr. Charles H. Schlichter, Elizabeth, chairman, and hospital relationships committee survey of outpatients, by Dr. Henry B. Decker, Camden, chairman. Dr. Harry R. North, Trenton, discussed a proposal to purchase a permanent home for the state society.

NEW YORK

New Tumor Clinic.—A tumor clinic has been organized at the Saratoga Hospital, Saratoga Springs, according to an announcement by the division of cancer control of the state department of health. Dr. Richard D. Bullard, Saratoga Springs, is executive officer of the new clinic, which is the thirty-sixth in the state, operated as a means of meeting the problem of cancer control in the state.

Annual Registration Due January 1.—Every practitioner of medicine and surgery in New York is required by law to apply annually, on or before January 1, to the secretary of the board of medical examiners for a certificate of registration, on application forms furnished by him, and to pay at that time a fee of \$2. The law authorizes the secretary of the board to permit secretaries of duly incorporated medical societies to act as his representatives to receive and transmit to him such applications and fees. Practitioners are liable to severe penalties for failing to register and for continuing in practice thereafter.

New York City

Third Harvey Lecture.—A. Baird Hastings, Ph.D., Hamilton Kuhn professor and head of the department of biological chemistry, Harvard Medical School, Boston, will deliver the third Harvey Lecture of the current season at the New York Academy of Medicine, December 19. His subject will be "The Electrolytes of Tissues and Body Fluids."

Symposium on Chemotherapy.—The Long Island College of Medicine presented a symposium on chemotherapy, November 13. Arnold H. Eggerth, Ph.D., associate professor of bacteriology, opened the program with a historical introduction and other speakers were:

- George W. Raiziss, Ph.D., Philadelphia, Mode of Action of the Sulfonamides.
- Dr. Elliston Farrell, assistant clinical professor of medicine at Long Island College, Toxic Reactions.
- Dr. Charles B. Jones, instructor in surgery, Long Island, The Sulfonamides in Surgery.
- Dr. Yale Kneeland Jr., assistant professor of medicine, Columbia University College of Physicians and Surgeons, The Sulfonamides in Pneumonia.
- Dr. Alfred Cohn, New York City Department of Health, The Sulfonamides in Gonococcal Infections.
- Dr. Josephine B. Neal, clinical professor of neurology, Columbia, The Sulfonamides in Meningitis.
- Dr. Lewis A. Koch, clinical professor of pediatrics, Long Island, The Sulfonamides in Pediatric Practice.

NORTH DAKOTA

Personal.—Dr. Bertha B. Brainard, Jamestown, was recently appointed in charge of the student health service at Oregon State College, Corvallis.—Dr. Elvin L. Sederlin, formerly of Laramie, Wyo., has been appointed health officer of Fargo, to succeed Dr. Harvey J. Skarshaug, resigned.

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in North Dakota is required by law to register annually, on or before January 1, with the secretary-treasurer of the board of medical examiners and at that time to pay a fee of \$5 if a resident of North Dakota, or \$2 if a nonresident. A practitioner may not lawfully practice if he has not registered. If he does so his license may be revoked and can be reinstated on the payment of unpaid fees and \$0.50 for each month of default.

OHIO

Dr. Hudson Goes to France.—Dr. Noel Paul Hudson, professor of bacteriology at Ohio State University College of Medicine, Columbus, has been granted a year's leave of absence to join a health commission of the Rockefeller Foundation to work in France. With other members of the commission Dr. Hudson was to leave late in October. He had previously served with the International Health Division of the Rockefeller Foundation. During the World War he served in France as a lieutenant in the Sanitary Corps of the Medical Department, U. S. Army.

Postgraduate Course in Toledo.—The Academy of Medicine of Toledo and Lucas County presented its annual postgraduate course of lectures, December 11-13, with Dr. Andrew C. Ivy, Nathan Smith Davis professor of physiology and professor of pharmacology, Northwestern University Medical School, Chicago, as the lecturer. Dr. Ivy's subjects included: physiologic changes in pregnancy, physiology of labor, the liver and biliary tract, water balance in health and disease, advances in diagnosis and therapeutic interest in the alimentary tract, hypertension, effects of various drugs on peripheral circulation, and heart failure.

PENNSYLVANIA

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Pennsylvania is required by law to register annually, on or before January 1, with the board of medical education and licensure in the department of public instruction and to pay a fee of \$1 or such fee as may be fixed by the department of public instruction. A practitioner who fails to register and who continues to practice is liable to a fine of from \$10 to \$100.

Special School to Extend Research.—The assets of the Devereux Schools, Devon, have been transferred to the Devereux Foundation, recently established by the founder of the schools, Helena T. Devereux. The foundation will continue to operate the schools and will increase the activities to include research, the further study and treatment of children through psychiatry and psychology and the establishment of scholarships. The schools have ten units and care for more than 200 children. The foundation will be under the direction of a board of trustees including Drs. Louis R. Kaufman, New York; Fred C. Aldridge, Wayne; Gabriel Henry Katz and Edward M. Westburg, Ph.D., of the Institute of the Pennsylvania Hospital, Philadelphia.

Philadelphia

Women's Cancer Forum.—The annual cancer forum presented to the public by the Women's Auxiliary to the Lankenau Hospital Research Institute, assisted by District No. 1 of the Pennsylvania State Nurses' Association, was held November 25-26 at the Bellevue-Stratford Hotel. Among the speakers were:

- Dr. Eugene P. Pendergrass, The Cyclotron—Newest Instrument to Study Cancer and Other Medical Problems.
- Otto C. Glaser, Ph.D., Amherst College, Amherst, Mass., The Relation of Biology and the Growth Problem to Cancer.
- Dr. Catharine Macfarlane, Further Report on the Reexamination of One Thousand Volunteers.
- Dr. Nathaniel Volney Ludwick, The Leukemias.
- Dr. Temple S. Fay, Further Observations on Refrigeration in Cancer.

Society News.—Drs. Frederick A. Bothe and Richard H. Meade Jr. addressed the Philadelphia Academy of Surgery, November 4, on "Mesenteric Adenitis" and "Healing of Abdominal Wounds in Perforated Peptic Ulcers" respectively. —Drs. Gabriel Tucker and Ernest A. Spiegel, among others, addressed the Philadelphia Laryngological Society, November 5, on "Hoarseness, Its Mechanism, Clinical Significance, Clinical Signs and Treatment" and "Reaction of the Labyrinth to Rhythmically Interrupted Currents" respectively. —Dr. John F. Fulton, New Haven, Conn., delivered the eighth S. Weir Mitchell Oration before the College of Physicians of Philadelphia, November 6, on "Neurology and War." —Speakers before the Obstetrical Society of Philadelphia, November 7, were Drs. Charles Mazer and Elkin Ravetz on "Effect of Combined Administration of Chorionic Gonadotropin and the Pituitary Synergist on the Human Ovaries," and Clifford B. Lull, "Pubertis Praecox Due to Ovarian Tumor."

RHODE ISLAND

Society News.—Dr. Shields Warren, Boston, addressed the Providence Medical Association, December 2, on "Medicolegal Aspects of Malignant Diseases." —Dr. John F. Kenney will address the Pawtucket Medical Association, December 19, on electrocardiography.

Personal.—Dr. Hilary J. Connor, Providence, has been appointed director of a new department for venereal disease control in the state health department. —Dr. Halsey DeWolf, Providence, has been appointed to the advisory state council of defense to coordinate state defense activities with those of the federal government and Dr. Albert H. Jackvony, Providence, has been made a member of the state selective service appeal board.

TEXAS

Annual Registration Due January 1.—Every practitioner of medicine and surgery holding a license to practice in Texas is required by law to register annually, on or before January 1, with the state board of medical examiners and at that time to pay a fee of \$2. If a practitioner fails to renew his registration within sixty days after January 1, his license is suspended.

VIRGINIA

Mental Hygiene Meeting.—Dr. David C. Wilson, Charlottesville, was elected president of the Mental Hygiene Society of Virginia at the annual meeting in Richmond, October 31. Guest speakers at the meeting were Drs. Frank J. Curran, New York, and Joseph E. Barrett, clinical director of Southwestern State Hospital, Marion, who discussed problems of the adolescent and Lawrence Kolb, U. S. Public Health Service, treatment and research in the field of mental disease.

Hospital Changes.—Dr. Grover C. Godwin, Sanatorium, N. C., has been named director of the Roanoke City Tubercular Sanatorium to succeed Dr. John E. K. Flannagan, resigned. —Dr. Samuel E. Hughes, medical director of the Hilltop Sanatorium, Danville, for many years, has resigned, it is reported. —Dr. Willard L. Quennell, has been appointed medical director of the Norfolk General Hospital to succeed Dr. Arthur H. Perkins, resigned.

GENERAL

Meeting of Insurance Physicians.—Dr. Donald B. Cragin, Hartford, Conn., was elected president of the Association of Life Insurance Medical Directors at the annual meeting in Boston, October 16-18. Dr. David E. W. Wenstrand, Milwaukee, became first vice president and Dr. William Bolt, New York, second vice president. Dr. Edwin G. Dewis, Newark, N. J., remains as secretary. Speakers, all of Boston, included Drs. Maurice B. Strauss, on "Disorders Due to Nutritional Deficiency"; Chester S. Keefer, "The Present Status of Chemotherapy in the Treatment of Infectious Diseases," and Merrill Moore, "Alcohol, a Medical Problem."

Southern Psychiatric Meeting.—Dr. Whitman C. McConnell, St. Petersburg, Fla., was named president-elect of the Southern Psychiatric Association at its annual meeting in Jacksonville, Fla., October 21-22, and Dr. Arthur J. Schwenkenberg, Dallas, Texas, was installed as president. Dr. James K. Hall, Richmond, Va., was elected vice president and Dr. Newdigate M. Owensby, Atlanta, Ga., reelected secretary. The 1941 convention will be in Nashville. Among speakers at the meeting were:

- Dr. Henry Mason Smith, Tampa, Fla., The Psychological and Economic Influence of Alcohol.
- Dr. Gilbert Christian Anderson, New Orleans, The Dental and Oral Basis of Certain Neuropsychiatric States.
- Dr. Francis J. Tartaglino, Washington, D. C., Psychotic Reactions Following Sulfanilamide Administration.
- Dr. Louis Michael Foltz, Lakeland, Ky., Involutional Melancholia and Its Connection to Gonadotropic Hormone Stimulation.
- Dr. Owensby, Homosexuality Corrected by the Pharmacologic Shock Method.

Neuropsychiatric Meeting in Milwaukee.—The Central Neuropsychiatric Association held its nineteenth annual meeting at the Hotel Pfister, Milwaukee, October 25-26, under the presidency of Dr. Percival Bailey, Chicago. Among the speakers were:

- Dr. Otto H. Foerster, Milwaukee, Self-Inflicted Lesions of the Skin.
- Dr. Max J. Fox, Milwaukee, Treatment of Bulbar and Upper Cervical Types of Poliomyelitis by Perivascular Drainage.
- Dr. Theodore L. Squier, Milwaukee, Emotional Factors in Allergic States.
- Dr. Andrew I. Rosenberger, Milwaukee, Observations on Treatment of Amyotrophic Lateral Sclerosis (Leukopolymyopathy) with Vitamin E.

A symposium on shock therapy was presented by Drs. Lloyd H. Ziegler, James A. Alston, Carroll W. Osgood, Michael Kasak, Harold T. Schroeder, Wauwatosa, and Jack L. Kinsey, Milwaukee. Officers elected were Drs. Louis J. Karnosh, Cleveland, president; Mabel G. Masten, Madison, Wis., vice president, and William C. Menninger, Topeka, Kan., secretary, reelected. The 1941 meeting will be in Detroit and Ann Arbor, Mich.

Influenza Epidemic.—An epidemic of mild influenza has been prevalent in California, reaching its peak during the first week of December. A total of 1,800 cases was reported for December 7, according to the newspapers. Thousands of persons have been stricken since the outbreak began in November. On December 5 the epidemic was said to have spread into

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Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 26, 1940 (delayed).

The Centenary of the British Medical Journal

Britons have been informed that the bombing of our cities and, at times, even villages is not due to any wish to destroy life and property but is really humanitarian, a means of bringing about a revolution and so ending the war! But, as foreign visitors confirm, all our activities continue with remarkable normality and calmness, though of course the war has altered some of our routine. The medical journals are a little shorter, because of the need to economize paper, but, excepting two local ones, they appear with their usual regularity. The *British Medical Journal* has not allowed the war to interfere with the celebration of its centenary. It publishes a reproduction of the "Introductory Address" of the first number (Oct. 3, 1840) of the *Provincial Medical and Surgical Journal*, which was its direct ancestor. The sentiments of the address are admirable and in no way out of date, but they are expressed with a verbosity which is now obsolete. In January 1857 the title *British Medical Journal* was adopted. The high standard, scientific and practical, always maintained by able editors and eminent contributors, is well known. In an editorial it is stated that this second year of the war finds Britain "an embattled country subject to perpetual air alarms and threatened with invasion, and the treatment of civilian air casualties is a matter of daily concern to doctors throughout the land. The future is obscure; but British hearts are stout." Many messages of congratulation from eminent members of the profession, from the editors of other journals published in the commonwealth and from the Editor of THE JOURNAL A. M. A. are published.

American and Canadian Physicians to Be Licensed for the Duration of the War

The government has made an order under the Emergency Powers Act, passed for the purposes of the war, enabling the General Medical Council to register for the period of the emergency Canadian and United States physicians. They will thus be able to join the Emergency Medical Service with the same privileges as British physicians. Previously we have never had medical reciprocity with the United States and only partial reciprocity with Canada, owing to difficulties which arose from the medical autonomy of the Canadian provinces. Applicants for the new registration must be British subjects or citizens of the United States, be of good character, and must hold some medical diploma recognized for the time being for the purposes of this order by the British General Medical Council as furnishing a guaranty of sufficient knowledge and skill for the efficient practice of medicine, surgery and midwifery.

Science and the War

In order to insure the fullest cooperation of scientific workers with the government in the national war effort a scientific advisory committee has been appointed after discussion with the Royal Society. The committee consists of the following, among whom medical science is represented: Sir William Bragg, president of the Royal Society; E. V. Appleton, F.R.S. (physicist), secretary of the Department of Scientific and Industrial Research; Sir Edward Mellanby, F.R.S. (physiologist), secretary of the Medical Research Council; Sir Edwin Butler, F.R.S., secretary of the Agricultural Council; Prof. A. V. Hill (physiologist), physical secretary of the Royal Society; Prof. A. G. Egerton, F.R.S., biologic secretary of the Royal Society.

The terms of reference of the committee are (1) to advise on any scientific problem referred to them, (2) to advise government departments on the selection of persons for particular lines of scientific inquiry or membership of committees on which scientists are required and (3) to bring to notice promising new scientific or technical developments which may be important in our war effort.

A Bombed Hospital

The following is an example of what hospitals have to go through: A bomb fell on an emergency hospital in south-eastern England, killing some patients who had been evacuated from bombed London hospitals. The bomb crashed through three wards, and many patients were buried amid tons of wreckage. The fire department freed some of them, and while the bombers were still overhead the nurses worked among the debris, bringing mattresses and administering morphine to trapped patients.

The Feeding of the Army

The Select Committee on National Expenditure has received a report from its subcommittee on army services recommending the greater use of canned foods. Evidence was received indicating the advantages of providing the army with more fruits and vegetables. The subcommittee considers that during the winter a position of extreme complexity and difficulty may arise, owing to the fact that numbers of troops will have to be accommodated in billets and hutsments and that efficient catering will play a conspicuous role in maintaining the physical condition and morale of the troops. Canned and prepared foods would give increased variety and in many cases supply the troops with food that merely requires heating, for which skilled cooks would not be required.

A Second Contingent of the American Hospital Unit

The second contingent of the American Hospital Unit, financed by the Allied Relief Fund, has arrived. The vessel in which it came encountered a violent Atlantic storm and as there was no ship's doctor the unit attended the casualties caused among the passengers and crew. The party consists of a surgeon and a physician who are brothers, a radiographer, four nurses and a laboratory technician. There is Dr. Henry Heyl, a 34 year old neurosurgeon, who has trained for eight years under Dr. Jason Mixer and Dr. Gilbert Horrax, leading neurosurgeons. His brother Dr. James Heyl specializes in internal medicine and research work. The radiographer, Mr. William Wykoff, was in Finland during the Russian invasion. He and one of the nurses made their way back to America through Germany and Lisbon.

Marriages

WILLIAM PROVINCE MCGUIRE, Winchester, Va., to Miss Dorothy Elizabeth Robinson of Glen Rock, N. J., at Ridgewood, N. J., October 19.

JOHN THORNTON MITCHELL, Miami, Fla., to Miss Marie Hammond of La Grange, Ga., in Fort Lauderdale, Fla., in October.

CLARENCE S. BOLENDER, Clearwater, Fla., to Mrs. Carrie Weaver Waddell of Cambridge City, Ind., September 18.

WILLIAM EDWARD STEINER, Savanna, Ill., to Miss Marie Melanie Kolbus of Chicago in September.

GROVER CLEVELAND WRENN, Siler City, N. C., to Miss Virginia Gaddy in Raleigh, October 20.

PLINY AUSTIN PRICE, Toledo, Ohio, to Miss Margaret Marie Harrigan of Columbus in October.

PHILLIP BROWER PARSONS, Charlotte, N. C., to Miss Annette Barnes of Elm City, October 12.

ERNEST DE WITT RICHARD PONZER to Miss Elizabeth Parkin, both of Chicago, September 21.

HENRY PLETCHER CLOSE to Miss Mary Dorothy Quinn, both of Philadelphia, October 1.

Deaths

Le Roy Long * Oklahoma City; Louisville (Ky.) Medical College, 1893; member of the House of Delegates of the American Medical Association, 1903, 1904 and 1920; demonstrator of genito-urinary diseases at his alma mater, 1894-1895; dean and professor of surgery, University of Oklahoma School of Medicine, 1915-1931; past president of the Oklahoma State Medical Association and the Oklahoma County Medical Society; member of the Western Surgical Association and of the American Association for the Surgery of Trauma; fellow of the American College of Surgeons; member of the state board of medical examiners from 1911 to 1915; served during the World War; surgeon, St. Anthony's Hospital; aged 71; died, October 27.

Walter Edward List, Cincinnati; Medical College of Ohio, Cincinnati, 1907; member of the Ohio State Medical Association; superintendent of the Jewish Hospital; formerly superintendent of the Minneapolis General Hospital; trustee of the American Hospital Association from 1935 to 1937; on the editorial board of *Hospitals*, the Journal of the American Hospital Association; fellow of the American College of Hospital Administrators; aged 54; died, October 26, of coronary occlusion.

Frederick Woltmann, Kampsville, Ill.; Hahnemann Medical College and Hospital, Chicago, 1903; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; member of the Illinois State Medical Society; served during the World War; aged 64; died, October 7, in the Veterans Administration Facility, Jefferson Barracks, Mo., of melanotic sarcoma.

Edwin Minor Huston * Dayton, Ohio; Medical College of Ohio, Cincinnati, 1896; past president of the Ohio State Medical Association and the Montgomery County Medical Society; formerly member of the board of education; for many years on the staff of the Miami Valley Hospital; aged 75; died, October 22, in Malone, N. Y., of carcinoma of the stomach.

George Washington Strickland, Roselle, N. J.; Long Island College Hospital, Brooklyn, 1895; member of the Medical Society of New Jersey; formerly member of the school board; aged 75; for many years on the staff of St. Elizabeth Hospital and Elizabeth General Hospital, Elizabeth, where he died, October 2, of cerebral hemorrhage and myocarditis.

Isadore Bernard Rothstein * Newark, N. J.; University and Bellevue Hospital Medical College, New York, 1923; member of the American Academy of Pediatrics; aged 40; on the staff of the Irvington (N. J.) General Hospital, Babies' Hospital-Coit Memorial and the Newark Beth Israel Hospital, where he died, October 22, of malignant nephrosclerosis.

Louis Charles Deane * San Francisco; Cooper Medical College, San Francisco, 1891; member of the Pacific Coast Ophthalmological Society; for many years visiting surgeon to the Stanford University Hospital; on the staff of the Mount Zion Hospital from 1912 to 1926; aged 69; died, October 17, of coronary occlusion and chronic myocarditis.

Frederick William Bailey, Manhasset, N. Y.; State University of Iowa College of Medicine, Iowa City, 1905; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; formerly on the staffs of St. Luke's and Mercy hospitals, Cedar Rapids, Iowa; aged 62; died, October 11.

Harry Clay Sharp, Lyons, N. J.; University of Louisville (Ky.) Medical Department, 1893; in 1909 delegate of the American Medical Association; served during the World War; at one time on the staff of the Indiana Reformatory, Jeffersonville, Ind.; on the staff of the Veterans Administration Facility; aged 70; died, October 31, of myocarditis.

Jacob Schultz, Middlesboro, Ky.; Hospital College of Medicine, Louisville, 1906; member of the Kentucky State Medical Association; past president of the Bell County Medical Society; on the staff of the Middlesboro Hospital; aged 60; died, October 3, in the Johns Hopkins Hospital, Baltimore, of septicemia and infection of the urinary tract.

Raymond Brewer Parker * Winthrop, Mass.; Harvard Medical School, Boston, 1912; chairman of the board of health and school physician; president of the staff of the Winthrop Community Hospital; served during the World War; aged 54; died, October 19, of coronary thrombosis, arteriosclerosis, chronic nephritis and hypertension.

Hugh Alexander Chisholm, Halifax, N. S., Canada; McGill University Faculty of Medicine, Montreal, Que., 1905; served during the World War; at one time inspector of health

of Nova Scotia and member of the department of pensions and national health; formerly port physician of Halifax; aged 57; died, September 25.

William John Bierer, Kittanning, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1897; member of the Medical Society of the State of Pennsylvania; past president of the Armstrong County Medical Society; county medical director; for many years a member of the school board; aged 67; died in October.

James Lawrence Thompson, Columbia, S. C.; Medical College of the State of South Carolina, Charleston, 1889; member of the South Carolina Medical Association and the American Psychiatric Association; on the staff of the South Carolina State Hospital; aged 86; died, September 24, of arteriosclerosis.

William Bruce Almon, Halifax, N. S., Canada; Halifax Medical College, 1899; associate professor of obstetrics emeritus at his alma mater, now the Dalhousie University Faculty of Medicine; formerly visiting physician, Infectious Disease Hospital; at one time health officer; aged 65; died, September 11.

Albert Alton Getman * Syracuse, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York, 1915; fellow of the American College of Physicians; on the staff of the General Hospital; aged 52; died, October 28, in the Strong Memorial Hospital, Rochester, of cerebral arteriosclerosis.

Albert Clark Benedict, Yonkers, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1871; member of the Medical Society of the State of New York; for many years police surgeon; formerly on the staff of St. Joseph's Hospital; aged 96; died, October 29.

George Andrew Sarchet, Mobridge, S. D.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1901; member of the South Dakota State Medical Association; served during the World War; on the staff of the Mobridge Hospital; aged 66; died, September 21, of carcinoma of the larynx.

Walter Redmon Pinnell, Mount Sterling, Ky.; University of Louisville (Ky.) Medical Department, 1907; member of the Kentucky State Medical Association; past president of the Montgomery County Medical Society; aged 54; died, October 2, in the Good Samaritan Hospital, Lexington, of nephritis.

Bruno Joseph Sawicki, Detroit; Toledo Medical College, 1913; Detroit College of Medicine and Surgery, 1917; member of the Michigan State Medical Society; served during the World War; aged 51; died, October 11, in the Mercy Hospital, Bay City, of injuries received in an automobile accident.

Simon Gunerus Gill, New Orleans; University of Louisiana Medical Department, New Orleans, 1878; at one time a pharmacist; formerly quarantine inspector for the state board of health at Port Eads, La.; aged 95; died, October 23, of malignant papilloma of the bladder and chronic myocarditis.

Francois X. L. de Martigny, Montreal, Que., Canada; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1893; served during the World War; formerly on the staff of the Hôpital Ste. Jeanne d'Arc; aged 68; died, September 28.

Henry Bettis Malone, Chester, S. C.; North Carolina Medical College, Charlotte, 1909; member of the South Carolina Medical Association; served during the World War; was chairman of the county board of health; aged 65; died, October 8, of bronchiectasis and heart disease.

Donald Wallace Skeel * Los Angeles; University of Southern California College of Medicine, Los Angeles, 1899; medical director of the Occidental Life Insurance Company; served during the World War; aged 67; died, October 11, of coronary thrombosis and arteriosclerosis.

David Kaufman, Altoona, Pa.; Jefferson Medical College of Philadelphia, 1908; member of the Medical Society of the State of Pennsylvania; served during the World War; aged 55; on the staffs of the Altoona Hospital and the Mercy Hospital, where he died, October 22, of leukemia.

Gustave A. Ozenne, Winfield, Ala.; University of the South Medical Department, Sewanee, Tenn., 1906; member of the Medical Association of the State of Alabama; aged 57; died, October 24, in a hospital at Birmingham of retroperitoneal hemorrhage and intestinal obstruction.

Abraham Turner Hubbell * Wood River, Neb.; Chicago Homeopathic Medical College, 1903; Northwestern University Medical School, Chicago, 1905; aged 62; associate member on the staff of St. Francis Hospital, Grand Island, where he died, October 18, of coronary embolism.

Ralph Kable Collins, New York; Johns Hopkins University School of Medicine, Baltimore, 1922; member of the staff of the International Health Division of the Rockefeller Foundation; aged 46; died, October 1, at the Rockefeller Institute Hospital of pulmonary embolus.

Howard Wilbert Nowell ☉ Brookline, Mass.; Boston University School of Medicine, 1911; instructor in pathology at his alma mater from 1911 to 1913 and associate professor from 1913 to 1915; aged 68; died, October 28, in Ogunquit, Maine, of chronic myocarditis.

John Aquaro, New York; Columbia University College of Physicians and Surgeons, New York, 1898; served during the World War; at one time inspector for the department of health, and physician on the staff of the department of correction; aged 64; died, October 15.

William Johnstone Thomson, Broadmoor, Colo.; Northwestern University Medical School, Chicago, 1899; member of the Colorado State Medical Society; served during the World War; aged 66; died, October 14, in the Glockner Hospital, Colorado Springs.

Samuel Augustus Scott, Eudora, Ark.; University of Louisville (Ky.) Medical Department, 1877; Medical Department of Tulane University of Louisiana, New Orleans, 1894; aged 87; died, October 14, in Vicksburg, Miss., of pernicious anemia and arteriosclerosis.

Clinton Durham Fife ☉ Dayton, Ohio; Western Reserve University Medical Department, Cleveland, 1921; fellow of the American College of Physicians; on the staffs of the Miami Valley and Good Samaritan hospitals; aged 45; died, October 24, of uremia.

Lorin W. Smith, Hastings, Minn.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; member of the Indiana State Medical Association; at one time mayor of Wabash, Ind.; aged 75; died, October 8, of chronic myocarditis and nephritis.

Gaston Torrance, Birmingham, Ala.; University of Virginia Department of Medicine, Charlottesville, 1897; member of the Medical Association of the State of Alabama and the Southern Surgical Association; aged 72; died, October 18, of pneumonia.

Archie L. Shanks, Hannibal, Mo.; Washington University School of Medicine, St. Louis, 1901; member of the Missouri State Medical Association; aged 65; on the staff of St. Elizabeth's Hospital, where he died, October 23, of coronary occlusion.

Leo Earle Wilson, Stamford, Conn.; University of Vermont College of Medicine, Burlington, 1928; member of the Connecticut State Medical Society; aged 37; died, October 13, of ruptured esophageal varices with hemorrhage and Laënnec's cirrhosis.

Dickson Leonard Moore, Columbus, Ohio.; University of Wooster Medical Department, Cleveland, 1892; member of the Ohio State Medical Association; for many years on the staffs of the Grant and Children's hospitals; aged 77; died, September 27.

Marian H. Frauenthal Sloane ☉ New York; University and Bellevue Hospital Medical College, New York, 1930; on the staffs of the Hospital for Joint Diseases and the New York Infirmary for Women and Children; aged 35; died, September 23.

Allen Gilbert Ireland ☉ Trenton, N. J.; Medical School of Maine, Portland, 1918; formerly member of the state department of public instruction; aged 40; died, October 23, in the University Hospital, Philadelphia, of glioma of the left temporal lobe.

William James Jolly ☉ Oklahoma City; Medical College of the State of South Carolina, Charleston, 1882; an Affiliate Fellow of the American Medical Association; fellow of the American College of Surgeons; aged 91; died, September 24.

Elliott Thompson Jett, Falmouth, Va.; University of Virginia Department of Medicine, Charlottesville, 1889; aged 71; died, October 17, in the Mary Washington Hospital, Fredericksburg, of strangulated inguinal hernia and intestinal obstruction.

Samuel Ellsworth Blair, Alford, Iowa; State University of Iowa College of Medicine, Iowa City, 1894; member of the Iowa State Medical Society; aged 73; died, October 8, in the McKennan Hospital, Sioux Falls, S. D., of coronary sclerosis.

Thomas H. Wood, Bell Buckle, Tenn.; University of Nashville Medical Department, 1886; member of the Tennessee State Medical Association; president of the Bedford County Medical Society; for many years mayor; aged 73; died, October 18.

James Coleman Fisher, Jefferson, Ohio; Rush Medical College, Chicago, 1889; on the board of trustees of Millikin University from 1904 to 1930; aged 82; died, October 27, in the Ingleside Hospital, Cleveland, of valvular heart disease.

Theodore Henry Smith, Detroit; Detroit College of Medicine, 1896; member of the American Urological Association; served during the World War; on the staff of the Harper Hospital; aged 65; hanged himself, September 30.

Wilmoth Osborne ☉ New York; University of Oregon Medical School, Portland, 1924; on the staff of the New York Hospital; aged 44; died, September 12, in the Presbyterian Hospital of metastatic carcinoma of the brain.

Leslie Guy Eastman Hazen, N. D.; Hering Medical College, Chicago, 1903; member of the North Dakota State Medical Association; past president of the North Dakota Sixth District Medical Society; aged 67; died, September 21.

Leonard William Brown, Indianapolis; Central College of Physicians and Surgeons, Indianapolis, 1903; member of the Indiana State Medical Association; aged 64; died, October 5, in St. Vincent's Hospital of coronary occlusion.

Robert Henry Martin, Magnetic Springs, Ohio; McGill University Faculty of Medicine, Montreal, Canada, 1896; member of the Ohio State Medical Association; aged 65; died, October 30, in the University Hospital, Columbus.

Jessica Royce Carleton, Ambala, Punjab, India; Woman's Medical College of Pennsylvania, Philadelphia, 1886; medical missionary; for many years director of the Philadelphia Hospital for Women; aged 78; died, October 23.

James Leslie Passmore, Detroit; Michigan College of Medicine and Surgery, Detroit, 1906; veteran of the Spanish-American and World wars; aged 60; died, October 19, in the Receiving Hospital of cerebral hemorrhage.

Chester Dare Lee, Donelson, Tenn.; Vanderbilt University School of Medicine, Nashville, 1914; superintendent of the Tennessee Home and Training School for Feeble-minded; aged 57; died, October 16, of cerebral hemorrhage.

Charles Frederick Roan ☉ Chicago; University of Illinois College of Medicine, Chicago, 1928; on the staffs of the Augustana Hospital and the Lutheran Deaconess Hospital; aged 41; died, October 12, of coronary thrombosis.

Alan Greenleaf Terrell, Riverhead, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1892; formerly health officer; aged 74; hanged himself, October 9, in Southampton.

Edward J. Murphy ☉ Philadelphia; Jefferson Medical College of Philadelphia, 1906; on the staffs of the Jewish Hospital, St. Mary's Hospital and the Germantown Dispensary and Hospital; aged 55; died, September 21.

Frederick Remington Johnson ☉ New York; Columbia University College of Physicians and Surgeons, New York, 1936; aged 32; was killed, September 18, in an automobile accident near New Milford, Conn.

Virgil Dark, Opelika, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; member of the Medical Association of the State of Alabama; aged 53; died, September 18, in Alexandria City.

Daniel H. Fondren, Maben, Miss.; Memphis (Tenn.) Hospital Medical College, 1893; member of the Mississippi State Medical Association; aged 71; died, October 13, in the Houston (Miss.) Hospital of heart disease.

Zachary Taylor Pinner, Pomaria, S. C.; Chattanooga (Tenn.) Medical College, 1905; member of the South Carolina Medical Association; aged 62; died, October 18, in a hospital at Columbia of pneumonia.

Raymond Clark Breece, Grand Rapids, Mich.; Michigan College of Medicine and Surgery, Detroit, 1905; served during the World War; aged 61; died, October 8, in the Michigan Soldiers' Home Hospital.

Anthony Joseph Villone, Quincy, Mass.; Tufts College Medical School, Boston, 1918; member of the Massachusetts Medical Society; aged 49; died, October 6, in the City Hospital of coronary thrombosis.

Richard Frederick Codrington, Richland, Mich.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1902; aged 85; died, October 25, in the Borgess Hospital, Kalamazoo, of cirrhosis of the liver.

Lee Alfred Hays, Columbus, Ohio; Eclectic Medical College, Cincinnati, 1910; served during the World War; aged 58; died, October 30, in the White Cross Hospital, Columbus, of cerebral hemorrhage.

DEATHS

JOUR. A. M. A.
Dec. 14, 1931

Clifford Gordon Engle * Henderson, Texas; Eclectic Medical College, Cincinnati, 1920; aged 47; died, October 14, in a hospital at Natchitoches, La., of injuries received in an automobile accident.

Thomas James O'Brien, Pawtucket, R. I.; College of Physicians and Surgeons, Baltimore, 1912; on the staffs of the Homeopathic and St. Joseph's hospitals, Providence; aged 51; died, September 22.

Chester Ambrose Wilkinson * Kendall, Mich.; Jefferson Medical College of Philadelphia, 1888; aged 78; on the staff of the Bronson Hospital, Kalamazoo, where he died, October 11, of heart disease.

John Charles Emme, Harlan, Ind.; Indiana University School of Medicine, Indianapolis, 1912; aged 50; died, October 25, in the Lutheran Hospital, Fort Wayne, of cardiovascular renal disease.

Laurence Clarke Swan * Beverly, Mass.; Harvard Medical School, Boston, 1907; served during the World War; aged 59; on the staff of the Beverly Hospital, where he died, October 2, of embolism.

Walter V. Lunsford, Pueblo, Colo.; Ensworth Medical College, St. Joseph, Mo., 1891; aged 85; died, September 9, in the Parkview Hospital of acute myocarditis and pulmonary tuberculosis.

Charles Benjamin Shotwell, Richmond, Mo.; Rush Medical College, Chicago, 1883; member of the Missouri State Medical Association; aged 83; died, October 12, of bronchopneumonia.

Margaret O'Hara, Smith's Falls, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1891; for many years Presbyterian medical missionary in India; aged 85; died, August 27.

Tallulah S. Tucker, Memphis, Tenn.; Indiana Eclectic Medical College, Indianapolis, 1887; aged 78; died, September 21, in the Baptist Hospital of cholecystectomy following jaundice.

Ransom Lee Carr, Rosehill, N. C.; Baltimore Medical College, 1907; formerly member of the state legislature and county health officer; aged 62; died, October 17, of arteriosclerosis.

Robert Eugene Forster, Chicago; Magyar Királyi Erzsébet Tudományegyetem Orvostudományi, Pecs, Hungary, 1923; aged 40; was found dead, October 30, of poison, self administered.

Gisela Von Poswik * Scranton, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1911; member of the American Roentgen Ray Society; aged 65; died, October 2.

Le Roy Willis, Central City, Ky.; Kentucky University Medical Department, Louisville, 1905; member of the Kentucky State Medical Association; aged 58; died, September 5.

Francis Lawrence Oswald, New York; University of the City of New York Medical Department, 1894; veteran of the Spanish-American War; aged 75; died, September 27.

Harvey Alfred Berkes * Los Angeles; Western Reserve University Medical Department, Cleveland, 1909; past president of the Hollywood Hospital; aged 58; died, October 30.

Raymond Eugene Robinson, Chicago; University Medical College of Kansas City, Mo., 1913; served during the World War; aged 50; died, October 2, of pulmonary embolism.

Charles Henry Curran, Springfield, Mass.; University of the City of New York Medical Department, 1886; died, September 10, of chronic myocarditis and arteriosclerosis.

James Rosser Bedford, Dahinda, Ill.; Rush Medical College, Chicago, 1881; Civil War veteran; aged 94; died, October 19, in Onaida of cerebral hemorrhage and pneumonia.

Charles E. Beitmen, Kendrick, Okla.; St. Louis College of Physicians and Surgeons, 1903; also a druggist; aged 73; died in October in Oklahoma City of cerebral hemorrhage.

James Alexander Murray, Victoria, B. C., Canada; Halifax (N. S.) Medical College, 1905; served with the Canadian Army during the World War; aged 59; died, August 27.

Frank Algan Duston, St. Stephen, N. B., Canada; Harvard Medical School, Boston, 1911; on the staff of the Chipman Memorial Hospital; aged 62; died, September 12.

Marion G. Wilbur, Chicago; Medical College of the State of South Carolina, Charleston, 1902; member of the Illinois State Medical Society; aged 68; died, October 8.

Eric Lafcadio Nye, Amarillo, Texas; University of Kansas School of Medicine, Kansas City, 1937; aged 30; died, October 24, of heart disease and pulmonary tuberculosis.

Frank Walter Shaw, Gimli, Man., Canada; University of Manitoba Faculty of Medicine, Winnipeg, 1920; aged 52; died, October 26, of hypertension and arteriosclerosis.

John R. Bolognino * New York; Regia Università di Torino Facoltà di Medicina e Chirurgia, Italy, 1905; aged 59; died, October 22, of coronary thrombosis.

Eugene Young Amerson, Roscoe, Texas; University of Texas Faculty of Medicine, Galveston, 1939; aged 25; was killed, October 6, in an automobile accident.

Herman George Rosenblum * Flint, Mich.; Toledo Medical College, 1913; served during the World War; aged 51; died, October 28, of myocarditis.

William S. Love, Wilber, Neb. (licensed in Nebraska in 1892); aged 90; died, September 30, in St. Elizabeth's Hospital, Lincoln, of arteriosclerosis.

William Park Myers, Anaheim, Calif.; Medical College of Ohio, Cincinnati, 1899 and 1906; aged 63; died, October 1, of hypertensive heart disease.

Louis William Eckels Jr., Louisville, Ky.; Kentucky University Medical Department, Louisville, 1906; aged 55; died, October 29, of pneumonia.

Arthur William West, San Antonio, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1919; aged 53; died, October 3.

Henry Michell De Werth, North Olmsted, Ohio; Cleveland Homeopathic Medical College, 1906; aged 60; died, October 21, of heart disease.

Orlando A. Hall, Webster City, Iowa; Eclectic Medical Institute, Cincinnati, 1876; aged 92; died, August 26, of cardiac vascular disease.

Cawood Johnson Carmichael * Knoxville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1902; aged 61; died, October 9.

Charles Henry Beadles, Oglesby, Ill.; Rush Medical College, Chicago, 1890; aged 73; died, October 2, in the Peoples Hospital, Peru.

John Ephraim Elliott, Toronto, Ont., Canada; Victoria University Medical Department, Coburg, 1884; aged 81; died, September 27.

Charles G. Main, St. John, N. B., Canada; McGill University Faculty of Medicine, Montreal, Que., 1891; aged 75; died, September 7.

James Holmes Barr, Yuba City, Calif.; Chicago Medical College, 1890; formerly county health officer; aged 82; died, September 9.

Alexander Jardine Hunter, Teulon, Man., Canada; University of Toronto Faculty of Medicine, 1895; aged 72; died, August 25.

James G. Pou, Courtland, Miss.; University of Louisiana Medical Department, New Orleans, 1871; aged 91; died, September 16.

Mary Gamble Bryson, La Jolla, Calif.; Trinity Medical College, Toronto, Ont., Canada, 1903; aged 66; died, September 4.

Hyuk Chong Liu * Honolulu, Hawaii; College of Medical Evangelists, Los Angeles, 1922; aged 47; died, September 23.

Julia M. Walton, Jackson, Mich. (licensed in Michigan in 1900); aged 93; died, September 15, of cerebral hemorrhage.

Donald McKay, Collingwood, Ont., Canada; University of Toronto Faculty of Medicine, 1889; aged 74; died, September 28.

G. E. Bigham, Ivey, Ga.; University of the South Medical Department, Sewanee, Tenn., 1898; aged 65; died, September 25.

Cornelius Herman Van Ravenswaay * Boonville, Mo. (licensed in Missouri in 1897); aged 69; died, September 29.

Lemuel Allen Carter, Bunnell, Fla.; Atlanta (Ga.) College of Physicians and Surgeons, 1909; aged 52; died, September 28.

Jacob Henry Siegel, Staten Island, N. Y.; Long Island College Hospital, Brooklyn, 1908; aged 57; died, October 24.

Alexander Moir, Hensall, Ont., Canada; Manitoba Medical College, Winnipeg, 1906; aged 66; died, September 12.

Franklin Beyersdorf, St. Helena, Calif.; Missouri Medical College, St. Louis, 1879; aged 87; died, September 13.

Frederick A. Luce, Cicero, Ill.; College of Physicians and Surgeons of Chicago, 1892; aged 84; died, October 2.

David Harold Karp, Rumson, N. J.; Long Island College Hospital, Brooklyn, 1908; aged 56; died, October 12.

John Nathan Thresh, Grand Bay, Ala.; Barnes Medical College, St. Louis, 1902; aged 66; died, October 14.

Correspondence

CLOSED METHOD OF TREATING COMPOUND FRACTURES

To the Editor:—I have just read with much interest the communication (THE JOURNAL, November 23, p. 1821) of Dr. De Groat of Detroit. All his references to the history of wound treatment are correct, but his account is still incomplete. In several of my contributions, going back to 1923, I have referred to the work of Ollier (1830-1900) in bone and joint surgery. As to wound treatment, actually he made no contribution whatever. All his suggestions about wound treatment had been anticipated by Magati (1579-1647) in Italy, Belloste (1654-1730) in France, John Hunter (1728-1793) in England and others.

The editorial in THE JOURNAL to which Dr. De Groat refers, and others relating to my work on the treatment of osteomyelitis, compound fractures and infected wounds, have to do not only with the treatment of wounds and fractures by infrequent dressings but with an entire program of preliminary immobilization, drainage operation, adequate immobilization in plaster of paris casts and infrequent dressings in the postoperative care. It is extremely important that this entire program be kept in mind, as the infrequent dressing method alone, while valuable in itself, is only a part of the program necessary for best results in cases of compound fracture.

In a recent discussion led by my associate Dr. Fritz Teal before the Boston Orthopedic Club (November 18) one of the members of the audience, Dr. Otto Herman, raised, among others, the following questions:

Q.—Do you ever have to do secondary wound suturing?

A.—We do no wound suturing in any case. The closing of contaminated pockets in any wound not only interferes with drainage but affords an opportunity in some cases for the development of anaerobic infections (gas gangrene, tetanus, and the like).

Q.—Does this Orr method stimulate granulation over bare bone areas (areas laid bare by injury)?

A.—In the early reduction, indirect skeletal fixation (or direct fixation in some cases) and infrequent dressing method that we employ, all these wounds heal from the bottom, as well as from the edges, by granulation. There are no pockets at all in the best cases and, while sinuses must occasionally be reopened, we almost never have to treat the wound by closure, skin graft or otherwise.

Q.—How do you treat compound fracture dislocation about joints?

A.—Such injuries are treated by immediate reduction, enlargement of wounds for drainage if necessary, petrolatum packs (into the wound but not into the joints), pins through adjacent bones and fixation of the limb in a cast.

Q.—Do you get infection at wire fixation points?

A.—We use rigid pins fixed in plaster of paris casts and have no irritation or infection either in the bone or in the skin.

Finally, our healed (or cured) cases have always constituted between 85 and 90 per cent of all our cases. The larger death and amputation rates in most reports are due usually to shock, to postoperative mixed infections due to dressings or to gas gangrene, most of which we avoid by the program I have proposed.

These questions indicate that even by such competent surgeons as Dr. Otto Herman, some of the points in my program (since 1923) are not fully appreciated. Obviously this is the case with Dr. De Groat. There is no reason whatever for associating Ollier's name with the infrequent dressing method. Many others have suggested that. The program which I propose, however, must be considered as a whole. It is different from any other treatment ever proposed for compound fractures, osteomyelitis and infected wounds in general.

H. WINNETT ORR, M.D., Lincoln, Neb.

To the Editor:—Dr. Albert De Groat suggests in a communication published in THE JOURNAL, Nov. 23, 1940, apropos of the editorial (THE JOURNAL, September 21, p. 1022) under the heading "Closed Method of Treating Compound Fractures and Infected Wounds," that the credit for the method belongs to Ollier of Lyons and should be referred to as "Ollier's method." The originator of the method was not Ollier but Alphonse Guérin.

He invented in the pre-Lister era the method of packing the wound thoroughly with cotton and bandaging it in a circular fashion sufficiently tight so as practically to accomplish immobilization. These bandages were left undisturbed for from twenty to twenty-five days. Guérin practiced this method on a wide scale at the Hôpital Saint Louis and accomplished a rate of recoveries truly miraculous for that period. Ollier introduced important modifications into the method of Guérin. Thus he sutured the stump after amputation and applied the cotton dressing above. He also applied Guérin's method in compound fractures with displacement of the fragments. In support of my statement I submit the following bibliographic references:

Chattelain, J. V.: *Mémoire sur l'emploi du coton et des pansements rares dans le traitement des plaies et ulcères*, *Rec. de mêm. de méd. mil.* 39: 61, 1836.

Courbet, A.; Alphonse Guérin; sa vie, son œuvre, Thesis, Paris, No. 45, 1913.

Alphonse Guérin, in *Biographisches: Lexikon der hervorragenden Aerzte aller Zeiten und Völker*, ed. 2, Berlin, 1930, vol. 2.

Hervey, A.: *Pansement à la ouate*, *Arch. gén. de méd.* 81: 641, 1871.

Medical Milestones, *M. Rec.* 150: 37 (July 5) 1939.

Rochard, J. E.: *Histoire de la chirurgie française au XIX^e siècle*, Paris, J. B. Baillière et fils, 1875.

Viennois: *Combinaison des appareils inamovibles avec les pansements isolants dans le but d'obtenir la réunion immédiate*, *Gaz. heb. de méd.* 18: 749, 1871.

GEORGE HALPERIN, M.D., Chicago.

PROSTIGMINE OF NO VALUE AS PREGNANCY TEST

To the Editor:—I wish to report my limited experience on the use of prostigmine in delayed menstruation. My results are not as favorable as those reported in the article of Soskin, Wachtel and Hechter in THE JOURNAL, May 25, on "Treatment of Delayed Menstruation with Prostigmine: A Therapeutic Test for Pregnancy."

Stimulated by the fine reports in the aforementioned article and the promotion of prostigmine methylsulfate by Hoffmann-

Results with Prostigmine Methylsulfate

Case	Friedman Urine Test	Prostigmine Methylsulfate, Ampules	Estradiol Benzoate, 2,000 Rat Units
1. V. N. aged 27; 14 days delayed; secundipara	Positive	3 x 2 cc. negative	No effect with daily doses
2. M. B. aged 22; 21 days delayed; primipara	Negative	Positive flow in 48 hrs. 2 cc.-2 cc.
3. S. A. aged 24; 5 days delayed; secundipara	Negative	Negative 3 x 2 cc.	Positive flow after 4 x dully dose
4. D. D. aged 21; 9 days delayed; secundipara *	Negative	Negative 1 cc.-2 cc.-1 cc.	Not tried

* Patient clinically pregnant after a few weeks and is observed pending delivery.

LaRoche, I decided to use the test on a small number of private patients. The 4 cases tabulated give sufficient indication that their conclusions in only a small series of 25 cases are incorrect. Four interesting variations occurred, tending to indicate that prostigmine cannot be relied on as a test in a presenting case for diagnosis. The authors' statement "If she fails to menstruate, pregnancy may be diagnosed with the same degree of accuracy as in the Friedman test" is not true.

In my first and second cases the results were confirming. My first patient gave a positive reaction to the Friedman test, with no response to prostigmine. The second had normal urine, and menstruation was produced with prostigmine. The results of the third and fourth cases disagreed. The third patient had normal urine which did not respond to prostigmine but did to estradiol benzoate. (The use of the latter I shall immediately explain). The fourth patient gave a negative reaction to a pregnancy urine test and no response to prostigmine but was found

to be pregnant clinically in a later examination. You will note four possible variations.

It will be noted that I used estradiol benzoate and it produced flow in a negative case and none in a positive one. I offer it as a suggestion in amenorrhea with a negative Friedman test. The technic I used was one ampule of 2,000 rat units daily for five doses. The flow will come during the injections or about two to four days after the last injection. How effective this treatment is I have not evaluated statistically.

ALEXANDER WINTER, M.D., New York.

"ILLUSTRATIVE ELECTROCARDIOGRAPHY"

To the Editor:—Some of the statements made by the reviewer of the book "Illustrative Electrocardiography" (THE JOURNAL, Sept. 21, 1940) are misleading. Some of the review presents debatable points on which I feel, on good authority, that our conclusions are much less theoretical and more logical than those of the reviewer.

The reviewer's criticism said: "It is questionable whether the attempt to locate the origin of the premature systole as stated on page 49 is correct." The great majority of recognized cardiologists agree with our interpretation (Nomenclature and Criteria for Diagnosis of Heart Disease, ed. 4, p. 128).

The review said: "It is doubtful whether the slight variation in the PR interval in plate 44 is worth mentioning." The variation is 0.02 second. This is certainly worth mentioning, as 0.02 second often means the difference between a normal record and a conduction block.

The review said: "The interpretation of plate 54 is wrong." Our conclusions were based on a comparison of records taken on a healthy young intern before and immediately following heavy exercise. The T wave prior to exercise was much smaller.

The reviewer said: "No useful purpose is served in showing the original lead 4 in plate 96, since this lead is no longer utilized." This is a misstatement of fact which no serious student of electrocardiography would uphold. True, the lead as such is no longer utilized, but, as the text explains, "A tremendous mass of literature has been published using the original fourth lead." Also a tremendous number of original fourth leads have been taken clinically. Furthermore, some of our noted authorities on the subject have incorporated the original fourth lead in their works and books. Both the research man and the clinician must know the basic picture from which precordial leads have evolved in order to evaluate properly the records of that time.

JULIUS BURSTEIN, M.D., New York.

CRYSTALLIZATION (?) OF METALS

To the Editor:—My attention has been called to a medicolegal abstract ("Malpractice: Liability for Injury to Patient from Nurse's Operation of Fluoroscope") in THE JOURNAL, September 28.

The National Bureau of Standards letter circular LC486, "Metals Do Not 'Crystallize' Under Vibration," has been prepared to answer the many inquiries we receive on this subject.

Members of the staff of the National Bureau of Standards are called on to examine many instances of fatigue failure in all sorts of structures. It is our experience that one fatigue failure in a certain part in a given structure which has been in use for a considerable time is all too likely to be followed by a number of like failures in the same part in other structures of the same kind which have given as long or longer similar service.

This likelihood is so great that it is frequently thought advisable in the case of a serious fatigue failure in one airplane to ground all airplanes of the same kind until they can

be examined to make absolutely sure that there is no cause to anticipate other failures of the same kind or, if cause is found, to remove it.

A roentgen ray examination is useless, since fatigue failures are not caused by crystallization.

The examination consists in looking for such surface defects as are mentioned in the letter circular, corrosion pits or craters, notches, abrupt changes in section, sharp reentrant angles, rough machined surfaces and the like, and in addition careful inspection for any fatigue cracks which may have started. For steel parts an inspection by means of divided magnetic particles, either as a dust or suspended oil (commercially known as Magnaflux), is now routine practice when fatigue cracks are feared.

If, as is implied in the report of this case, the failure was a fatigue failure, and serious personal injuries might result from like failures in other fluoroscopic tables of the same kind, it would seem to me very desirable that all tables of that particular model and other models having the same mechanical design should be carefully examined as just outlined.

If a second accident of the same kind should occur, it would seem to me, in view of this previous failure, difficult to maintain that the maker and users of the apparatus had exercised proper care to prevent it.

L. B. TUCKERMAN, Washington, D. C.
Assistant Chief, Mechanics and Sound Division,
National Bureau of Standards.

[COMMENT.—The medicolegal abstract that prompted this correspondence involved liability for injuries sustained by a patient because of the failure of a fluoroscopic table to operate properly. A representative of the manufacturer of the table investigated the accident and testified in court that a broken pin was the causal factor and further that the "parts showed it was broken from crystallization." Among other contentions the plaintiff urged that the defendants had not from time to time caused the gear box to be taken off, the gears to be removed or the pin to be taken out of its socket and placed under roentgen rays to determine whether crystallization had occurred. For further details with respect to this case readers are referred to the abstract of it, which was published in THE JOURNAL, September 28, page 1128.—ED.]

DEATH OF DR. R. FORTESCUE FOX

To the Editor:—Your London staff correspondent in his letter of August 11 (THE JOURNAL, September 21) ends with mention of the recent death of England's leading balneologist, Dr. Robert Fortescue Fox. Unfortunately, he mixed the latter's fine life record with that of a relative, Dr. Richard Hingston Fox, noted in another special field of practice.

Fortescue Fox was one of Britain's pathfinders in physical medicine, his manual on "Physical Remedies for Disabled Soldiers," to refer to only one of his authoritative writings, proving of great help to those of us stationed in hospitals during the first world war.

The concluding statement of your overseas correspondent, "A great pioneer of physical therapy, he experienced much of the disappointment of the reformer in a world which will not share his enthusiasms," may apply to conservative England but no longer to North America. Over here, aided by the American Medical Association, our profession grows ever more aware of the usefulness of modern physical treatment methods.

In later years the activities of Fortescue Fox were largely directed to thalassotherapy and balneotherapy, his editorial charge of the *Archives of Hydrology* bringing him in touch with physicians of many countries interested in spa treatment and, especially, rheumatic conditions.

Long acquaintance and admiration for the many sided talents of this leader in our profession is my warrant for this brief tribute.

A. BERN HIRSH, M.D., New York.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

FIRE AND EXPLOSIVE HAZARD IN PRESENCE OF OXYGEN ADMINISTRATION

To the Editor:—I recently gave an order at the hospital for continuous steam inhalation and oxygen administration by catheter. The sister on duty told me that doctors in another hospital had forbidden her to administer oxygen and steam inhalation in the room at the same time. She also said that persons visiting patients receiving oxygen were not permitted to smoke. Is there any reason for such a rule? Is there any danger of explosion when a person smokes in the same room in which oxygen is being administered? If there are any contraindications to these various procedures please tell me about them and also the mechanism involved.

V. V. Anderson, M.D., Del Norte, Colo.

ANSWER.—The 20 per cent oxygen in atmospheric air is responsible for the burning of all fuels and other oxidizable substances. As the percentage of oxygen is increased, the ease with which combustion occurs increases rapidly, while the degree of heat necessary for ignition becomes less. Oxygen itself does not burn or explode from contact with a source of heat. Although a glowing heat source is necessary to ignite some materials (sheets, blankets and the like) even in high oxygen atmospheres, some substances (such as lint or organic dusts) may burn or even explode in the presence of high oxygen concentrations when exposed to moderate degrees of heat. In particular ether, vinethene, cyclopropane and ether, exhaled by the patient in the hours immediately after operation, are a great danger.

Steam is usually produced by stoves or electrical heating elements. Such sources of heat should be banned from the room of a patient receiving any form of oxygen therapy. Simultaneous administration of oxygen and steam is not harmful of itself, provided the source of heat for the latter is remote. Steam from a radiator or stem pipe or jugs of hot water is quite safe.

Smoking must be prohibited in the room where oxygen is being administered. The glowing pipe, cigar or cigaret might suddenly flare into violent flame if brought close to the patient or if air currents carried excess oxygen toward the smoker.

VACCINE VIRUS AND IMMUNITY TO POLIOMYELITIS

To the Editor:—Is there any experimental evidence or are there statistical data that vaccinia confers any immunity against infantile paralysis? Such a phenomenon seems possible to me. Vaccinia causes immunity to variola and to herpes virus. Moreover, mouse infantile virus protects monkeys against lethal doses of monkey virus. Might not extensive smallpox vaccination be worth trying as a protective measure in an epidemic of infantile paralysis?

Richard E. Stifel, M.D., Cleveland.

ANSWER.—There is no evidence that the vaccine virus confers immunity against poliomyelitis. This subject has been investigated on several occasions. In the early years, soon after the discovery of and isolation of the virus (Thompson, O.: *Berl. klin. Wchnschr.* 49:63, 1912, 51:309, 1914; *Ztschr. f. Immunitätsforsch.* 14:198, 1912), neither immunity nor alterations in the course of experimental disease were produced when the virus of vaccinia and the poliomyelitis virus were applied together on the skin. Thompson believed, however, that the poliomyelitis virus proliferated in the pustules. Hurst and Fairbrother (*Brit. J. Exper. Path.* 12:17, 1931) also concluded that the neurovaccine had no power to modify the poliomyelitis lesions in the nervous system regardless of the route of inoculation. It is known that school children who are still active in their immunity against vaccinia are just as susceptible to attacks of poliomyelitis as are children not vaccinated. These data were obtained in the Chicago and Illinois epidemics of 1936 and 1937. The status of the new cotton rat virus (Armstrong and Jungeblut) as an immunizing agent against the monkey virus has not been determined conclusively as yet.

In summary, there is no evidence that vaccination against smallpox leads to protection in an epidemic of infantile paralysis. The only positive ray of hope in protection against this disease appears to come from the recent work showing that the virus is contained in sewage and intestinal discharges of

carriers and active cases, including both paralytic and nonparalytic types. This would indicate the usual precautions which are used in the prevention of wholesale dissemination of intestinal borne diseases, including boiling of water and the prevention of congregations of children where an aqueous medium may disseminate the disease, such as swimming pools. Chlorination and other chemicals appear to have little effect on the virus.

HEREDITARY DYSTROPHY OF HAIR AND NAILS

To the Editor:—I wish to inquire about nonsyphilitic baldness showing for three direct generations. There is scarcely a trace of hair and only rudimentary finger and toe nails. 1. How often is this found? 2. What may be the cause? 3. Are such individuals usually normal physically and mentally? 4. Is it similar to albinism? 5. Kindly give the history of this condition.

M.D., Iowa.

ANSWER.—1. Cases of this type are rare and should therefore be studied and accurately recorded. The heredity should be worked out as clearly as possible, the condition of the hair, nails, teeth, skin and eyes carefully noted, and a general examination of the patient for any indications of metabolic or endocrine anomalies should be made.

2. Consanguinity of the parents has been recorded in several instances and of course this adds to the probability of the occurrence of this defect in the children. Many cases have no such easy explanation and in some the case recorded is the only one in the family, so far as known. Henry Joachim (*Dystrophy of the Hair and Nails in Six Generations, Ann. Int. Med.* 10:400 [Sept.] 1936) reports this dystrophy in nineteen of forty-two individuals in six generations of a family. In one of his cases there had been defective vision since childhood but the eye clinic reported only that the visual field of the left eye was contracted. One authority states that the partial types are of dominant heredity, while another holds that the generalized type is recessive. This is one of the reasons for urging the study of all such cases.

Besides the involvement of the teeth and nails, so common an accompaniment of alopecia congenita, eye defects, webbing of the fingers and toes, atrophy of parts of the skin, epidermolysis bullosa and alopecia areata have been recorded. J. N. Hyde, early among American writers on this condition (*Congenital Alopecia as an Expression of Atavism, J. Cutan. Dis.* 27:1, 1909), cited cases in his own practice, one of webbed fingers and toes and another of opaque patches in the retina. He also mentioned Eschner's case with exaggerated myopia and white areas in the retina. Jäckli (Ein Fall von infantiler Poikiloderma, [Atrophodermia Reticularis cum Incontinentia Pigmenti] kombiniert mit Alopecie, Mikrodentie und frühseiger Cataracta Complicata, *Monatschr. f. Kinderh.* 78:73 [March 24] 1939) reports a case of severe atrophy of the skin and bilateral juvenile cataract in a little girl whose hair, normal at birth, fell out before she was 3 weeks old and never regrew. One of Hyde's patients had xeroderma, and he mentions this complication in the case of Guilford and Luce. He also mentions Wende's case with atrophy of the finger tips and congenital epidermolysis bullosa.

3. All authorities agree that these patients show mental and physical defects, other than those mentioned in connection with the baldness, no more frequently than individuals without the ectodermal dystrophies.

4. The only similarity between this group of ectodermal defects and albinism is that both are hereditary. Albinism is a defective formation of pigment in the skin, iris and hair, often accompanied by mental and physical weakness. There is no other abnormality of the skin, hair, nails or teeth; thus albinism differs sharply from the condition mentioned in the query.

5. By "the history of this condition" it is inferred that the prognosis is meant. The best way to answer this question is to get a biopsy of the scalp. If only the merest traces of hair follicles are found, as recorded by some investigators for their cases, no hope can be given that hair will grow later. If, however, many bed hairs are seen, there is a possibility that the hair can be restored. Every encouragement should be given the patient to continue for a long time the use of local stimulants to the scalp such as are used for other types of alopecia. Ultraviolet rays in erythema doses given once or twice a week, depending on the amount of irritation caused, are an excellent stimulant; but the acquired resistance soon makes it necessary to give long treatments. Then chemical irritants may succeed it; a mixture of equal parts of tincture of iodine, chloral hydrate and phenol can be painted on once a week. One part of phenol with four parts of lactic acid is also effective. Solutions of cresol in alcohol can be used in increasing strength, beginning

with 25 per cent and going to 90 per cent. Chrysarobin in varying strength is also recommended; but great care must be exercised that none of the preparation gets into the eyes. It is well not to use these irritants at once over the whole scalp but to try out their effect first on a small area. During intervals of rest from the strong treatment milder stimulants may be used, salicylic acid and sulfur in ointment, mercurials in ointment or alcoholic solution.

COMBINED FEVER AND ROENTGEN THERAPY FOR CANCER

To the Editor:—I understand that some work is being done on carcinoma at Rochester, N. Y., with the use of high voltage roentgen therapy combined with a special type of short wave therapy. Can you furnish me with any information about this?

A. L. Goldwyn, M.D., South Ozone Park, N. Y.

ANSWER.—Studies on the combined effects of high voltage roentgen therapy and artificial fever on carcinoma are under way at Rochester, N. Y., and probably elsewhere too.

The summative effects of the two radiations x-rays and heat appear to be more destructive to the carcinoma and normal structures than either alone. Since the dosage values are not well understood the experiments have been restricted to hopeless cases. The delayed effects (telangiectases, edema, cutaneous degeneration, and the like) seem to be more marked, probably because of the summative effect.

The following dosage has been used with safety, though it should not be attempted by any one not well versed in both irradiation technic and fever treatment technic: Daily for six days 250 roentgens is given in the usual manner for any one port. On the third day in this schedule a five hour fever bout at 41.5 C. (106.7 F., rectal temperature) is administered and at the end of the fever, while the body temperature is up, that day's x-ray treatment is given. A second fever bout of one hour (or more if the patient is not too much intoxicated by the tumor destruction) is given on the fifth day with the x-ray treatment again administered at its end. Several portals may be treated simultaneously except that great caution must be exercised not to overtreat (i. e. not over 1,800 roentgens given to any one skin area) within a given course. Courses have been repeated in six months without catastrophe, although the damage to the skin was considerable.

At present this method is purely experimental and is not advocated for general use until its merits are more clearly defined.

MINERAL METABOLISM AND ELECTROLYTE BALANCE

To the Editor:—I am interested in the relation of mineral salt metabolism or, let me say, electrolyte metabolism and disease. As a matter of routine in medical conditions I elicit a dietary history from my patients and I find that the incidence of faulty eating and the preparation of foods is appalling. I should therefore like to know if any reports have been published on investigative work giving this relationship quantitatively and qualitatively. In the literature there is often mentioned the term "electrolyte pattern." Just exactly what is meant by that term? References on this most interesting subject will be greatly appreciated.

B. C. Baron, M.D., Munising, Mich.

ANSWER.—The best outline of this subject is probably to be found in the recently published monograph by A. T. Shohl on "Mineral Metabolism" (published by the Reinhold Publishing Corporation), reviewed in THE JOURNAL, April 27, page 1691. The phrase "electrolyte pattern" is subject to considerable individual interpretation. However, in general it refers to the complex interrelations of the ions of electrolytes such as the direct relation between sodium and chlorine in the tissues and the inverse relation of sodium and potassium. A good discussion for the interested physician may be found in an article by A. M. Butler on "Electrolyte and Water Balance" (*New England J. Med.* 220:827 [May 18] 1939).

COAL OIL INSTILLATIONS FOR ULCERATIVE COLITIS

To the Editor:—Has the use of coal oil by instillation in chronic ulcerative colitis been tried in competent hands? If so what quantity is used and what results have been obtained?

M.D., California.

ANSWER.—From twelve to fifteen years ago coal oil instillations into the rectum received intensive trial in cases of amebic dysentery. At the time this was used in the treatment of amebiasis and amebic colitis it was also employed in other types of chronic ulcerative colitis. It was found to be too irritating and was soon abandoned as having no great value and possibly associated with some hazard. Coal oil is irritating to the skin and so when it was being instilled it was found necessary to grease the parts about the rectum with petrolatum. The amount instilled was about a pint. Injections were given every second day for a period of twenty-eight days.

POSSIBLE ARSENIC IN MILK AND ABORTION

To the Editor:—What form of arsenic preparation is used for spraying weeds and grass? If cattle should eat the grass which has been sprayed with an arsenic preparation would arsenic be found in the cow's milk in sufficient quantity to cause an acute poisoning with severe diarrhea and a miscarriage in a woman about four months pregnant? A woman claims that such a case has occurred. The cows that ate this sprayed grass died. The cows were milked a few hours after eating the grass and the woman drank this milk. A few hours later she had severe diarrhea and abdominal cramps. She was about four months pregnant. She miscarried and has been in poor health since.

Bernard Patrick, M.D., Corinth, Miss.

ANSWER.—There are several forms of arsenic for spraying weeds and grass—sodium arsenate, sodium arsenite, calcium arsenate and lead arsenate. In the South large amounts of calcium arsenate are used, particularly on cotton fields. There is no indication in this query what form of arsenic was used. If arsenic is eaten, some of it may appear in the milk so that it is possible that some arsenic could be obtained in this way and arsenic may produce diarrhea and cramps. That this diarrhea might produce an abortion is possible, but without further evidence on the subject one cannot say more than that it is possible.

ALCOHOL BY WEIGHT AND BY VOLUME

To the Editor:—In recent months there have been frequent references to 70 per cent alcohol by weight and the greater effectiveness of this concentration as an antiseptic. What would be the volumetric equivalent of this concentration?

M.D., Illinois.

ANSWER.—There can be no constant volumetric equivalent for 70 per cent alcohol by weight unless three variables are controlled:

1. Temperature. Alcohol is so expansible that 70 Gm. of it when warm occupies a larger volume than the same 70 Gm. when cool; water, on the other hand, has a relatively low coefficient of temperature expansion. Consequently 70 per cent by weight (that is, 70 Gm. of alcohol plus 30 Gm. of water) at 15 C. is equivalent to about 76.9 per cent by volume, whereas at 30 C. it is equivalent to about 82.5 per cent by volume.

2. Reaction contraction. When alcohol and water are combined, the resultant solution contracts with production of heat and the total volume decreases further as the solution cools. Hence it makes a difference whether alcohol and water are both measured separately before mixing or whether only the alcohol is measured and water is added to bring the total volume up to a certain level.

3. Alcohol content of commercial alcohol. Different lots of commercial alcohol have been found to vary between 95 and less than 92 per cent by volume.

If these three variables are not appreciated and controlled, it is possible that the volume per cent equivalent of "70 per cent alcohol by weight" may lie anywhere between 75 and 84. Or, to put it another way, 76.9 per cent by volume (or any other set figure) as ordinarily prepared may miss by a considerable margin being 70 per cent by weight. The reason for the discrepancy is that alcohol solutions by weight are unaffected by these variables and therefore are absolutely uniform. A somewhat fuller discussion of this matter is contained in an article entitled Ethyl Alcohol as a Germicide, by Dr. Philip B. Price, in the *Archives of Surgery* 38:528 (March) 1939.

HOT FOODS AND GASTROINTESTINAL CANCER

To the Editor:—Is there any method of preventing cancer of the stomach and bowels? Are too hot drinks and food a factor in causing it?

M.D., Pennsylvania.

ANSWER.—There is no known method of preventing cancer of the stomach and intestine. Hot foods have been suspected as having an etiologic relationship to cancer of the stomach but there is no positive evidence to prove this relationship. Many observers believe that hot and irritating foods constitute one factor in the development of gastric cancer but the relative importance of this factor is not definitely known.

TESTS FOR HOMOSEXUAL TENDENCIES

To the Editor:—In The Journal of September 28, 1940, on page 1122, I notice a reply to an inquiry about possible homosexual tendencies. I should like to suggest in addition to the routine psychiatric examinations and textbooks that are recommended the utilization of projective tests. Examination by means of the Rorschach test and the Szondi test could easily give much more complete and adequate information than any formal psychiatric examination could yield—that is, provided the tests are given by some person fully qualified to administer and interpret them.

Milton H. Erickson, M.D., Eloise, Mich.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examination of boards of medical examiners and boards of examiners in the basic sciences were published in *THE JOURNAL*, December 7, page 2019.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, February 10-12. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written*. Various centers, Feb. 20. Final date for filing application is December 21. *Oral*. Part II. Cleveland, May 31-June 1. Final date for filing application is April 1. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Parts I-A and I-B, Feb. 17. Final date for filing application is Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Part II, Groups A and B, Cleveland, May 28-June 1. Final date for filing application is March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral*. Cleveland, May or June. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written*. Cleveland, June 1-2. Final date for filing application is May 1. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, March 30-31, following the Region I meeting of the American Academy of Pediatrics. Chicago, May 18, following the Region III meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY: *Oral*. Cleveland, May 30-June 1. Final date for filing application is April 15. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

Indiana June Report

Dr. J. W. Bowers, secretary, Indiana State Board of Medical Registration and Examination, reports the written examination for medical licensure held at Indianapolis, June 18-20, 1940. The examination covered fifteen subjects and included 100 questions. An average of 75 per cent was required to pass. One hundred and eighteen candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
College of Medical Evangelists.....	(1940)		1
Yale University School of Medicine.....	(1939)		1
Loyola University School of Medicine.....	(1940, 3)		3
Northwestern University Medical School.....	(1940)		1
Rush Medical College.....	(1939)		1
University of Illinois College of Medicine.....	(1940, 2)		2
Indiana University School of Medicine.....	(1938), (1939), (1940, 100)	102	
University of Louisville School of Medicine.....	(1940, 2)		2
Johns Hopkins University School of Medicine.....	(1938)		1
Columbia University College of Physicians and Surgeons	(1940)		1
University of Oregon Medical School.....	(1939)		1
Marquette University School of Medicine.....	(1940)		1
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1937)		1

Washington July Report

Mr. Nelson N. Vaughan, secretary, Department of Licenses, reports the written examination for medical licensure held at Seattle, July 15-17, 1940. The examination covered 7 subjects and included 70 questions. An average of 60 per cent in each subject was required to pass. Thirty-five candidates were examined, all of whom passed. Twenty-six physicians were licensed to practice medicine by reciprocity and 8 physicians so licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Stanford University School of Medicine	(1939)		87.8*
George Washington University			84.3
Loyola University School of Medicine			82.2, 83.3
Northwestern University Medical School	(1938) 82.1, 92.1, (1940) 81.1, 85.54		87.
Rush Medical College.....	(1921) 80.6, (1937) 82.1, (1939)		79.5
University of Illinois College of Medicine.....	(1940)		79.87
Indiana University School of Medicine.....	(1933)		73
University of Michigan Medical School.....	(1934) 82.6, (1936)		85.3,
(1939) 85.3			
Washington University School of Medicine.....	(1939)		78.1
Creighton University School of Medicine.....	(1939)		70.8
Columbia University College of Physicians and Surgeons	(1939)		86.3
University of Oregon Medical School.....	(1939) 81, 83.2, 84, 85.3, 85.3, 89.3		81, 83.1,
McGill University Faculty of Medicine.....	(1939)		79
Medizinische Fakultät der Universität Wien.....	(1934)		78
Universität Heidelberg Medizinische Fakultät.....	(1909)		81.5
Universität Bern Medizinische Fakultät.....	(1937)		76.1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists.....	(1938)		California
Stanford University School of Medicine.....	(1937)		California
University of California Medical School.....	(1936)		California
Loyola University School of Medicine.....	(1936)		Missouri
Northwestern University Medical School.....	(1939)		California
Rush Medical College.....	(1937) Oregon, (1938), (1939)		California
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1925)		Maryland
University of Minnesota Medical School.....	(1928), (1940)		Minnesota
St. Louis University School of Medicine.....	(1937)		Missouri
Washington University School of Medicine.....	(1932), (1933)		Missouri
Creighton University School of Medicine.....	(1938), (1939, 2)		Nebraska
University of Nebraska College of Medicine.....	(1932), (1939, 2)		Nebraska
Cornell University Medical College.....	(1937)		Oregon
University of Oklahoma School of Medicine.....	(1939)		Oklahoma
University of Oregon Medical School.....	(1936)		Oregon,
(1938) California, Minnesota			
University of Wisconsin Medical School.....	(1937)		Wisconsin

School	LICENSED BY ENDORSEMENT	Year Grad.	Year Endorsement of
College of Medical Evangelists.....	(1937), (1940)	N. B. M. Ex.	
University of Kansas School of Medicine.....	(1933)	N. B. M. Ex.	
Duke University School of Medicine.....	(1937)	N. B. M. Ex.	
University of Oregon Medical School.....	(1937), (1939)	N. B. M. Ex.	
University of Pennsylvania School of Medicine.....	(1936)	N. B. M. Ex.	
Marquette University School of Medicine.....	(1935)	N. B. M. Ex.	

* This applicant has completed four years' medical work and will receive the M.D. degree on completion of internship. License has not been issued.

† License has not been issued.

Tennessee September Report

Dr. H. W. Qualls, secretary, Tennessee State Board of Medical Examiners, reports the written examination for medical licensure held at Memphis, Sept. 25-26, 1940. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Twenty-seven candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Rochester School of Medicine and Dentistry	(1940)		83.7
Marberry		138	85.3
University		140	82.7,
83.5, 86.1, 86.2, 86.5, 86.7, 87.1, 87.3, 87.7, 87.7, 88, 88.5, 88.8			
Vanderbilt University School of Medicine.....	(1939)		84

Thirteen physicians were licensed to practice medicine by endorsement from August 5 through October 11. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Year Endorsement of
College of Medical Evangelists.....	(1939)		California
University of Georgia School of Medicine.....	(1938)		Georgia
State University of Iowa College of Medicine.....	(1938)		Iowa
Tulane University of Louisiana School of Medicine.....	(1919)		Louisiana
Johns Hopkins University School of Medicine.....	(1933)		N. Carolina
Harvard Medical School	(1939)		B. M. Ex.
Washington Univ			Missouri
New York Home			
Hospital	(1933)		New Jersey
Duke University School of Medicine	(1928)		Minnesota
Temple University School of			Penna.
Baylor University College of			Texas
Univ. of Virginia Department			Virginia

Vermont June Report

Dr. W. Scott Nay, secretary, Vermont State Board of Medical Examiners, reports the written examination for medical licensure held at Burlington, June 11-13, 1940. The examination covered 12 subjects and included 90 questions. An average of 75 per cent was required to pass. Eighteen candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Vermont College of Medicine.....	(1938)		85.3,
(1939)* 88.9, (1940)* 86.2, 86.6, 87.1, 87.1, 87.8, 88, 88.1, 88.6, 88.9, 89.3, 90, 90.4, 91.8, 92.9			
Universidad Central de España Facultad de Medicina. Madrid	(1933)		75.1

Six physicians were licensed by endorsement from February 26 through August 3. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Year Endorsement of
College of Medical Evangelists.....	(1938)		Wisconsin
Tufts College Medical School.....	(1938)		N. B. M. Ex.
Columbia Univ. College of Physicians and Surgeons	(1914)		New York
Cornell University Medical College.....	(1932)		N. B. M. Ex.
University of Vermont College of Medicine.....	(1937), (1939)		N. B. M. Ex.

* Licenses have not been issued.

Book Notices

Graduate Medical Education. Report of the Commission on Graduate Medical Education. Cloth. Pp. 304. Chicago: University of Chicago Press, 1940.

The Commission on Graduate Medical Education was organized in 1937 as an offshoot of the Advisory Board for Medical Specialties, which felt that it was more representative of the different interests involved than any other body. The commission's activities were financed by the Rockefeller Foundation, the Carnegie Foundation, the Josiah Macy Jr. Foundation and some smaller contributions from other groups. Concerning internship it concludes:

1. The internship should be regarded as a part of the basic preparation for either beginning the general practice of medicine or undertaking advanced training in a specialty.
2. The internship should provide a real educational experience and a period of clinical responsibility under supervision that is designed to complete the clinical clerkship of the medical course.
3. The internship should be an important responsibility of the staff and should be under the direction of those members who are competent to provide the necessary instruction.
4. The internship should be a joint responsibility of the medical schools and of those hospitals that can provide a satisfactory completion of the fundamental preparation for medical practice.

Of residencies it says:

1. The residency should be the most satisfactory method of graduate training for specialized fields of practice.
2. The residency should be organized as a real educational experience provided by qualified teachers who are willing to assume responsibility for adequate instruction.
3. The residency should provide preparation in the sciences basic to the specialty as well as sufficient clinical experience, under supervision, to ensure real competence.
4. The residency should be a joint responsibility of medical schools and of those hospitals able to provide residencies of a satisfactory educational character.

The following are stated to be the basic principles of postgraduate medical education:

1. Postgraduate medical education should aim to keep the physician abreast of current knowledge in his present field of practice.
2. Postgraduate medical education, as defined in this report, should not attempt to qualify a physician for entering a specialized field of practice.
3. Postgraduate medical education divides itself into two independent categories which should be clearly differentiated; namely,
 - (a) Instruction for general practitioners.
 - (b) Instruction for those who are already qualified as specialists.
4. Postgraduate medical education should be offered only by those who are qualified to provide satisfactory instruction.
5. Postgraduate medical education should be coordinated by existing agencies in each state that are concerned with the health and medical care of the population.

This report has been criticized primarily because of its point of view. It has been charged that it represents a concept that the family doctor is merely an agent to direct his patient to a specialist. Today most of the physicians of the United States are in general practice. Unfortunately that very fact makes them less prominent in the groups of physicians who concern themselves with committees, councils and similar bodies that spend much of their time in discussions of medical education. The *Journal of the Michigan State Medical Society* has urged that a commission of general practitioners be organized to establish their point of view as to the principles which should underlie the training of interns. Some hospitals are beginning to recognize the validity of this criticism by the appointment of general practitioners to membership on their staffs and also by the establishment of residencies in general practice. Graduate medical education is still in what might be called an early experimental stage. Fortunately, this fact is recognized by most of the bodies which are concerned in the field and even the standards set by the certifying boards are not yet to be considered as the ultimate in each of these fields. The contribution of the Commission on Graduate Medical Education may be classified as "work in progress." The conditions change so rapidly that most of the tabular data which make up the appendix are already obsolete.

Allergiya i desensibilizatsiya. Pod redaktsiyei D. E. Alperna. L'allergie et la désensibilisation. Cloth. Price, 11 rubles. Pp. 217, with illustrations. Kharkov: Izdanie Ukrainskogo Instituta Eksperimental'nogo Meditsiny, 1940.

This small volume, published by the Ukrainian Institute of Experimental Medicine, contains brief reports on experimental and clinical studies in allergy and desensitization by Prof. D. E. Alpern and his co-workers. Alpern makes a distinction between specific and nonspecific desensitization. The first consists in creating within the organism a resistance to the antigen by immunobiologic action in the presence of antibodies. By nonspecific desensitization is meant the reduction of the exaggerated reactivity by means other than immunobiologic, namely, through the intervention of the regulatory systems of the organism, its metabolism and so on. There are chapters dealing with animal experiments and clinical trial of histamine, of ultrashort waves and of intermedin. Alpern claims to have obtained this hormone containing extract of the pars intermedia of the hypophysis long before Zondek (1932) described intermedin containing the melanotrophic hormone. He describes his method of obtaining the hormone from the hypophysis of small and large horned cattle. Several chapters are devoted to the effect of intermedin. Its effectiveness is determined by the extent to which allergy participates in a given pathologic state. The greater the allergic factor, the more effective is the intermedin. The latter was always effective in shock attending blood transfusion, in allergic disorders of the nasal mucous membranes, in phlyctenules, in recurrent rheumatism and in other allergic diseases. The work is in Russian with a synopsis in French accompanying each chapter.

Progress in Medicine: A Critical Review of the Last Hundred Years. By Iago Galdston, M.D. With a foreword by Henry E. Sigerist, M.D. Cloth. Price, \$3. Pp. 347. New York & London: Alfred A. Knopf, 1940.

Interesting himself in philosophies more than in events and personalities, the author has produced here a historical meditation concerning medical progress ostensibly only in the last century but in reality covering much more in point of time. His approach is reminiscent of Singer rather than of Clendening, Haggard or Major, whose historical essays for lay readers bid fair to become lasting contributions to this field of medical literature. He objects to "history viewed in the light of its heroes" because the lapses between the times of heroic individual achievements appear to be dark ages or voids. "History viewed as the progression of ideas has no dark ages" the author says in his introduction.

Proceeding on this theory, he opens with a review of "Preludes to Pasteur." Tracing the evolution of man's conceptions as to the causes of disease from Homer's description of the plague of the mules and the swift dogs which was ultimately communicated to man and attributed to the displeasure of Phoebus Apollo with Agamemnon, he sketches swiftly the outlines of development to the era of Pasteur, Koch and their compatriots and followers, with emphasis on the flow of thought and the growth of ideas and understanding rather than on the men through whom the ideas are implemented. As he states in his introduction "Ideas . . . do not progress by themselves. They have need for vehicles, human beings. We never confront a disembodied idea. There is always a man to express it, to cherish it, to defend it, to propagate it. In that respect ideas and human life have this in common, that each man receives his from another, to pass on, better or worse, but never to create independently."

From the pre-Pasteur era he traces the progress of medical thought through the era of those whom he calls the pasteurians, whose thinking was along microbian lines, to the challenge of nutrition problems, the rise of glandular knowledge, mental hygiene and psychiatry from Mesmer to Freud, a century of clinical progress, and a closing chapter entitled "Whither Medicine?" This is a prognosis for medicine in the scientific, not the economic, realm. The author's forecast is perhaps best represented, as far as brief quotations can represent it, in the following passages: "It is none too optimistic to believe that during our very lifetime 'some great truth has been loosened' in medicine, a truth that holds the proper precinct of medicine to be life, not death, that deems its primary concern to be health

not disease, that looks to the safeguarding of the man rather than to the conquest of the malady." However, as to the imminence of achievement of this "loosened truth" he says "The time . . . is not ripe, though medicine is, for the widespread practice of personal preventive medicine. I say medicine is ripe, but its ripeness is not full blown. Medicine today is not only adding much to its knowledge but is summing up much of what it has gathered into larger concepts and broader understanding. . . . But we do have more parts to put together." His final summation is in the words of Cicero: "Man never come closer to the gods than in giving health to men."

The book is thoughtful and thought provoking. It is not light reading, yet it is not hard reading, thanks to the author's broad acquaintance with medical and cultural literature, his individuality of style and the richness of his vocabulary. It is heartily recommendable for the physician and the thoughtful lay reader.

Textbook of Public Health. By W. M. Frazer, O.B.E., M.D., Ch.B., Medical Officer of Health, City and Port of Liverpool, and C. O. Stallybrass, M.D., Ch.B., D.P.H., Deputy Medical Officer of Health, City and Port of Liverpool. (Formerly Hope and Stallybrass.) Tenth edition. Cloth. Price, \$6.50. Pp. 504, with 64 illustrations. Baltimore: William Wood & Company, 1940.

The present edition of this standard work is thorough in all aspects of the subject and as complete a textbook on public health as the graduate student could desire. The obvious comparisons between the English and American methods are interesting, especially the section on milk production and inspection. Apparently pasteurization is not nearly as widespread a procedure in the British Isles as it is in the United States. The chapters on industrial hygiene, water, sewage disposal and housing are progressive and represent the modern trend of thought. Health officers in the United States have much to learn from the planned housing programs of Britain, and the various pages devoted to proper dwellings are of value and importance. Of additional interest is the chapter pertaining to marine hygiene, a subject that is frequently neglected in the average book on public health. The chapter on meteorology perhaps overemphasizes the effects of climate. Maternity and child welfare and school medical service are minutely described, including plans and diagrams of child welfare clinics. The absence of a separate chapter on public health nursing might be considered a defect. A departure from the usual is noted in the chapter on hospital administration, an oft neglected part of public health administration. This excellent volume closes with a chapter on medical aspects of civil air defense which is timely and well written. The book is thoroughly indexed.

Clinical Urology. By Oswald Swinney Lowesley, A.B., M.D., F.A.C.S., Director of the Department of Urology (James Buchanan Brady Foundation) of the New York Hospital, New York, and Thomas Joseph Kirwin, M.A., M.S., M.D., Attending Surgeon of the Department of Urology (James Buchanan Brady Foundation) of the New York Hospital. Volumes I and II. Cloth. Price, \$10, per set. Pp. 898; 899-1684, with 370 drawings by William P. Didusch. Baltimore: Williams & Wilkins Company, 1940.

In the development of this work, planned primarily for the medical student and general practitioner, the authors have followed classic arrangement by beginning with the general diagnostic procedures, including a chapter on history taking and physical examination, and then considering the organs of the urogenital tract in anatomic sequence from without inward. The first volume covers the external genitalia, with a special chapter on gonorrhea, and includes all the tissues through the prostate gland. The second volume is concerned with the bladder, the ureters and the kidneys, and there is a concluding chapter on radium and roentgen therapy of the genito-urinary tract.

Exceptional in this book are the magnificent illustrations by Didusch, of which there are a tremendous number both in black and white and in colors. Exceptional also is the readability of the type, which makes study of the book a veritable pleasure for the eye. The work is one of the most practical that is available, and the information particularly with regard to treatment is succinct and definite. The numerous side headings and center headings in various type make the acquiring of information relatively simple because the book falls naturally into excellent

outline form. So rapidly has chemotherapy developed in recent years that the book is already a little behind times as far as concerns some of the newer sulfonamide derivatives. Indeed, the book includes an extraordinary spelling of sulfathiazole. Nevertheless the volume contains references to periodical literature as late as February 1939. As a guide to the general practitioner these volumes may be recommended for their practicality and for their well considered didactic expression.

Problemy teoreticheskoy i prakticheskoy meditsiny. Leksii po usovershenstvovaniyu vrachev. Sbornik sedmoy. Otvetsstvennyy redaktor: S. Ya. Shumarov. [Problems of Theoretical and Practical Medicine. Postgraduate Lectures for Physicians. Seventh collection.] Boards. Price, 7 rubles. Pp. 272, with illustrations. Moscow: Izdatie Gosudarstvennogo Tsentralnogo Instituta Usovershenstvovaniya Vrachey, 1938.

This volume, in Russian, contains a series of lectures delivered in a ten day review course offered by the Central Postgraduate Institute. The ten day program was arranged so that each lecture presented a more or less complete review of the present status of a problem with emphasis on the contributions of Soviet medicine. The most prominent representatives of Soviet medicine were invited to participate. Preference was given to physiologic problems. On reading some of these lectures the reviewer felt that either the average Soviet doctor was head and shoulders above an average American physician or that the lectures went over their heads. They read in fact as an advanced seminar in physiology. Perusal of the titles alone is sufficient to indicate their highly theoretical nature. Thus, "The Modern Status of the Localization of Nervous Functions," "The Problem of the Center and the Periphery in the Physiology of Nervous Activity," "The Cortex and the Work of Internal Organs," "Chemical Nature of Ferments."

The Chinese Way in Medicine. By Edward H. Hume. Cloth. Price, \$2.25. Pp. 189, with 9 illustrations. Baltimore: The Johns Hopkins Press, 1940.

This book falls into three parts. The first deals with the universe and man in Chinese medicine and is a summary of the views of Chinese philosophers whose teachings afford the philosophical basis for Chinese medical procedures. These include the cosmic philosophy of Lao-tse with its two opposed forces, Yin, the negative, or female, and Yang, the positive, or male; the kwei or animal spirit, and the shen or intellectual spirit, both acquired during fetal life from the parents. Childbirth is a period of great susceptibility to spirits, and mental disturbances are due to excitement of the shen; hence exorcism by the cock, whose kinship with the sun confers on the blood of that bird subtle powers over the mind. The vegetable kingdom is also beset by spirits. The pine, cypress, peach and fungi possess the magic ling. Tao, the Way of Nature, gave rise to the belief in immortality, the Happy Islands, and indirectly to the elaborate systems of breathing, diet and physical exercises conducive to longevity. The mineral world also had its place in Chinese medicine, and gold, jade and pearls their place in medical lore. The second part is devoted to a review of the medical classics of the Chinese, in which are traced the rise of the elaborate use of the pulse in diagnosis, the development of herbals, the elaboration of anesthesia and surgical practice, and vaccination. The third part enumerates the distinctive contribution from Chinese medicine. The animistic, cosmic and medicamentous approach to disease are interesting historically but the last is most fruitful. Their empiric methods led to the use of the lining of the pig's stomach in anemia, the use of marine algae in thyroid disease, and of fish livers in scrofula and lung diseases. The use of poisonous reptiles and of the pills of eight poisons belong with that of the cicada and of jade more in the field of magic than of medicine. The important contributions are the origin of medicinal libraries and of medical monographs such as those on leprosy, venereal disease, smallpox, beriberi, obstetrics, gynecology and ophthalmology. Among medicaments of proved value used in Chinese medicine are stramonium, deer's horn (for calcium), Ephedra vulgaris, musk, iodine from seaweed, toad venom, chaulmoogra oil, tang kwei from *Cryptotaenia canadensis*, from which eumenol is derived, anthelmintics, fish oils and arsenic. Physical therapy is found in acupuncture and moxa, in the art of breathing and in physical exercises.

Mosquito Control: Practical Methods for Abatement of Disease Vectors and Pests. By William Brodbeck Herms, Sc.D., and Harold Farnsworth Gray, Dr.P.H. Cloth. Price, \$3.50. Pp. 317, with 60 illustrations. New York: Commonwealth Fund; London: Oxford University Press, 1940.

This handy book on mosquito control is an exhaustive study of the principles underlying the problem and the actual methods of abatement. Beginning in the introduction with a brief historical sketch of the origin of control, the work continues with the brief discussion of the cost of malaria from an economic point of view. State laws are reviewed and various nonofficial agencies for mosquito abatement are described. The various methods of control are described in great detail, as is also their adaptation to various types of land to be treated. An interesting chapter written with a sense of dry humor rarely seen in scientific textbooks is that on mosquito control by use of fish. The special features of the problem in urban and rural areas are described and the problem of the mosquito in the airplane and the military phases are not neglected. Considerable emphasis is placed on the education of the public in order to maintain interest and support for the carrying on of the work. Appendixes, dealing with the distribution of the anophelines and their larval habitats and a classification of methods, together with a selected bibliography, make it an extremely handy reference book. The authors have been actively associated with mosquito control work on the west coast for thirty years and the book will serve as a valuable guide for all those engaged in any aspect of mosquito abatement.

Synopsis of the Principles of Surgery. By Jacob K. Berman, A.B., M.D., F.A.C.S., Assistant Professor of Surgery, Indiana University School of Medicine, Indianapolis. Fabrikoid. Price, \$5. Pp. 615, with 274 illustrations. St. Louis: C. V. Mosby Company, 1940.

As the title indicates, this is another synopsis of the principles of surgery. Yet this one is much different from all the others on the subject and is probably the best that has been the privilege of the reviewer to see. The essential and most valuable feature of the book is that it is written with the idea of correlating the basic sciences with the fundamental principles of surgery. This the author accomplishes in a novel manner. The body of the text contains a discussion of the standard principles of surgery which are found in almost every textbook, while in footnotes, nearly as extensive as the text itself, he covers the related and pertinent facts of anatomy, pathology, biochemistry and physiology. Though the discussions are necessarily brief, the subject matter is covered completely and well. There is a tremendous amount of information between the covers of this volume, all of which is abreast of the time. The book is written in clear, simple style. It is attractively printed and contains a large number of excellently reproduced photographs and line drawings which enhance the value of the text. The book is highly recommended for surgeons as well as students for whom it was intended.

Clinical Dental Roentgenology: Technic and Interpretation Including Roentgen Studies of the Child and Young Adult. By John Opple McCall, D.D.S., F.A.C.D., Director, the Murry and Leone Guggenheim Dental Clinic, New York, and Samuel Stanley Wald, D.D.S., F.A.C.D., Head of the Department of Diagnosis and Roentgenology, the Murry and Leone Guggenheim Dental Clinic and School for Dental Hygienists. Cloth. Price, \$5.50. Pp. 319, with 1,046 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

This book is by teachers of dentistry, intended for practicing dentists and for radiologists or other physicians interested in dental roentgenology. The pages on technic call for clarification and condensation and chapter II, on electricity and roentgenology, merits no serious consideration by readers; but the bulk of the work, which deals with diagnosis, is excellent and is recommended without reservation to physicians desirous of improving and modernizing their ability to interpret dental roentgenograms. The anatomy of the teeth and jaws at all ages from fetal to adult life is described, and certain concepts of development that have become established among orthodontists are convincingly disputed. Periapical lesions, unerupted teeth, salivary duct stones and infections, tumors and injuries of the jaws are well described and illustrated. In addition to these familiar subjects there are discussed many others not so well known to physicians, such as growth phenomena, dental caries and periodontal disease.

Miscellany

PROPOSED ADDITIONS AND DELETIONS FOR THE UNITED STATES PHARMACOPEIA

Herewith is the report of the Subcommittee on Scope of the U. S. Pharmacopeia, Twelfth Revision. It consists of (a) a list of articles not formerly described in the Pharmacopeia but now recommended for inclusion in the U. S. P. XII and (b) a list of articles official in the U. S. P. XI but not recommended for admission to U. S. P. XII (commonly spoken of as "deletions").

ARTICLES NOT FORMERLY PHARMACOPEIAL NOW RECOMMENDED FOR THE U. S. P. XII

Absorbent Gauze	Picrotoxin
Absorbent Gauze, Sterile	Picrotoxin Solution (for injection)
Adhesive Absorbent Compress	Potassii Chloridum
Antipneumococcus Serum (the new monograph to cover all types)	Quinine Hydrochloride
Calaminae Preparata	Quinine Hydrochloride with Ethyl Carbamate Solution (for injection)
Calcium Mandelate	Riboflavin
Dextrose Solution (for injection 50 per cent)	Ringer's Solution
Dextrose (50 per cent) and Sodium Chloride (30 per cent) Solution (for injection)	Serums, Dry and Liquid forms authorized for all U. S. P. Serums
Elixir Cardamomii Compositum	Surgical Silk and other Surgical Sutures
Elixir Iso-Alcoholicum	Surgical Silk and other Surgical Sutures Sterilized
Elixir Phenobarbitali	Syrupus Ammonii Mandelatis
Elixir Terpinii Hydratis	Syrupus Glycyrrhizae
Ethyl Carbamate	Syrupus Rubi Ideaei
Gas Gangrene Antitoxin (to include types now used)	Telluriae Aminopyrinae
Gauze Bandage	Tetanus Toxoid
Glycocol (Amino Acetic Acid)	Tetrachloroethylene
Immune Serum for Scarlet Fever, Human	Theobromine with Sodium Acetate
Immune Serum for Measles, Human	Totaquinine
Immune Globulin (Placenta Extract) Human	Transfusion Normal Plasma, Human
Lotio Calaminae	Transfusion Normal Syrum, Human
Lotio Calaminae Phenolata (2 per cent Phenol)	Trichloroethylene
Magnesium Trisilicate	Urea
Oleum Hippoglossi (Halibut)	Vitamins A and D in Oil (Cod Liver Oil Strength)
Oubain	Zinc Peroxide

The following additional items, needed as "pharmaceutic necessities," must be added as new admissions:

Compound Spirit of Cardamom	Raspberry Juice
Cudbear	Spirit of Bitter Almond
Oil of Caraway	Tincture of Cudbear
Oil of Cardamom	

ARTICLES OFFICIAL IN THE U. S. P. XI, BUT NOT ADMITTED TO THE U. S. P. XII, COMMONLY SPOKEN OF AS "DELETIONS"

Acetum Scillae	Merbaphenum
Acidum Aceticum Dilutum	Mistura Opii et Glycyrrhizae Composita
Acidum Acetylsalicylicum	Oleum Santali
Acidum Sulfuricum Aromaticum	Pancrreatinum
Aconitum	Paraffinum
Albumini Tannas	Pepsinum
Ammonii Benzoas	Pilocarpinae Nitras
Ammonii Bromidum	Pilulae Aloes
Ammonii Salicylas	Podophyllum
Arseni Triiodidum	Potassii Chloras
Asafoetida	Pulvis Ipecacuanhae et Opii
Bismuthi Subgallas	Pulvis Sennae Compositus
Calcii Bromidum	Pyrogallol
Calcii Creosotas	Quinina
Cannabis	Resina Podophylli
Cantharis	Santoninum
Capsicum	Scilla
Carbo Activatus	Serpentaria
Carbromalum	Sodii Acetas
Ceratum Cantharidis	Spiritus Aethylis Nitritis
Cinchona	Spiritus Chloroformi
Colchici Semen	Strychninae Nitras
Copaiba	Sulfonethymethanum
Creosoli Carbonas	Sulfur Lotum
Creosotum	Syrupus Ferri Iodidi
Dichloramina-T	Syrupus Scillae
Emplastrum Cantharidis	Terebentum
Emulsio Asafoetidae	Theobromina cum Sodii Salicylate
Extractum Cannabis	Tinctura Aconiti
Extractum Nucis Vomicae	Tinctura Cantharidis
Ferrum	Tinctura Capsici
Fluidextractum Belladonnae Radicis	Tinctura Cinchonae Composita
Fluidextractum Cannabis	Tinctura Colchici Seminis
Galla	Tinctura Ferri Chloridi
Guaiacol	Tinctura Kino
Hydrargyri Iodidum Flavum	Tinctura Scillae
Iodoformum	Tinctura Valerianae
Kino	Tinctura Veratri Viridis
Liquor Ammonii Acetatis	Unguentum Gallae
Liquor Ferri Chloridi	Valeriana
Liquor Ferri Tersulfatis	Veratrum Viride
Magma Ferri Hydroxidi	
Massa Hydrargyri	

Physicians are encouraged to send comments on the foregoing proposals either to the Chairman of the Pharmacopeia Revision Committee, Dr. E. Fullerton Cook, Forty-Third Street and Woodland Avenue, Philadelphia, or to the Editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Basic Science Law (Arkansas): Constitutionality and Applicability to Chiropractors.—The legislature of Arkansas in 1915 enacted a statute creating a state board of chiropractic examiners and required it to examine prospective chiropractors in the subjects of anatomy, physiology, symptomatology, chemistry, hygiene, chiropractic principles and diagnosis. In 1929 a basic science law was enacted in Arkansas which requires every applicant desiring a license to practice the healing art or any branch thereof to pass an examination in the basic sciences—anatomy, physiology, chemistry, bacteriology and pathology—and present to the licensing agency a certificate to that effect, issued by the state board of examiners in the basic sciences, before he may be permitted to take a further examination for the particular branch of the healing art which he desires to pursue. This law excepted from its application dentists, nurses, midwives, optometrists, chiropodists, barbers, cosmeticians and Christian scientists. By reason of these statutory provisions, the plaintiff, the Arkansas Medical Society, petitioned the Pulaski chancery court for an injunction (1) to restrain the defendant state board of chiropractic examiners from issuing licenses to practice chiropractic to any applicants who failed to present certificates showing satisfactory completion of the required examination in the basic sciences and (2) to enjoin two individual chiropractors from practicing chiropractic under invalid licenses issued to them by the state board of chiropractic examiners without their having complied with the basic science law. From an order of the court denying the petition, the plaintiff appealed to the Supreme Court of Arkansas.

The defendants contended that the basic science law does not apply to the practice of or the licensing to practice chiropractic and that so far as it attempts to regulate such licensing or practice it constitutes an unreasonable and unconstitutional interference with the right to practice chiropractic. In support of this contention the defendants argued that bacteriology and pathology, two of the subjects in which applicants for licensure to practice the healing art are required by the basic science law to take examinations, were neither essential to nor connected with the practice of chiropractic. With this contention, however, the Supreme Court of Arkansas could not agree. The legislature, said the court, believed it proper that all persons seeking a license to practice the healing art should have a knowledge of, among other subjects, bacteriology and pathology, and we cannot say their inclusion as to chiropractic was unreasonable, arbitrary and without any relation to such practice. Bacteriology is defined by Webster as "The science which deals with the study of bacteria. It is a branch of botany, but some of its most important practical relations are with hygiene, medicine and agriculture." Certainly bacteriology has some relation to the practice of chiropractic since "some of its most important practical relations are with hygiene," a subject in which a prospective chiropractor is required by the chiropractic practice act to take an examination. Pathology is defined as "The science treating of diseases, their essential nature, causes and development, and the structural and functional changes produced by them." In reply to the defendants' argument that the subject of pathology was not related to the practice of chiropractic because chiropractors do not diagnose or treat disease but merely locate "the nerve pressure of the spinal column" and make proper adjustments to relieve that pressure, the court said: "If he does not treat diseases, what does he treat? Does he manipulate the vertebrae of a well person just for the pleasure of such well person? There would be no excuse for any regulatory chiro-

practic laws, if they were not engaged in treating disease." In the judgment of the court, the basic science law does apply to the practice of and the licensing to practice chiropractic, which is a branch of the practice of the healing art, and applicants for license must successfully pass examinations in the basic sciences before the basic science board of examiners as a prerequisite to eligibility for examination before the chiropractic board.

Furthermore, continued the court, the basic science law does not abridge the rights and privileges of chiropractors but simply places additional requirements on the qualifications for practice. It merely regulates the practice of chiropractic but does not ban it. The fact that the basic science law excepts from its operation dentists and certain others does not constitute, as the defendants claimed, an arbitrary and unreasonable classification.

The Supreme Court of Arkansas concluded that the basic science law is constitutional, and so it reversed the judgment and remanded the case with directions that the injunction be granted. An appeal to the United States Supreme Court was dismissed for want of a substantial federal question.—*Stroud et al. v. Crow et al. (Ark.)*, 136 S. W. (2d) 1025; 61 Sup. Ct. 17.

Society Proceedings

COMING MEETINGS

- American Association for the Study of Neoplastic Diseases, Baltimore, Dec. 19-21. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.
- American Student Health Association, Ann Arbor, Mich., Dec. 27-28. Dr. Ralph I. Canuteson, University of Kansas, Lawrence, Kan., Secretary.
- Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otolological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.
- Middle Section, American Laryngological, Rhinological and Otolological Society, Chicago, Jan. 27. Dr. Walter H. Theobald, 307 North Michigan Blvd., Chicago, Chairman.
- Society of American Bacteriologists, St. Louis, Dec. 27-29. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
- Southern Section, American Laryngological, Rhinological and Otolological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.
- Western Section, American Laryngological, Rhinological and Otolological Society, San Francisco, Feb. 1-2. Dr. Robert C. Martin, 384 Post St., San Francisco, Chairman.

THE AMERICAN RHEUMATISM ASSOCIATION

Seventh Annual Meeting, held in New York, June 10, 1940

DR. LORING T. SWAIM, Boston, Secretary

(Continued from page 2026)

The Familial Epidemiology of Rheumatic Fever

DR. MAY G. WILSON, DR. RALPH E. WHEELER, and MORTON D. SCHWEITZER, PH.D., New York: Taking the family as the unit for epidemiologic study, the relation of environment, contagion and heredity to the spread of rheumatic fever in 112 families was considered. It was found that the frequency of rheumatic fever did not differ significantly in families of varying economic levels ranging from dire poverty to middle class comfort, although rheumatic recurrences were less frequent among children living under relatively favorable environmental conditions. No evidence was obtained that rheumatic fever is passed back and forth from case to case in the family. Simultaneous attacks in the household were no more frequent than might have been expected from chance association. The incidence of recurrences bore no direct relation to the size of family or the number of rheumatic members and seemed to represent recrudescences of existing disease rather than new infections. Unlike most acute communicable diseases, the age of onset for children presumably exposed within the family (secondary cases) was not earlier than for those exposed "outside" the family (primary cases). No evidence was obtained to indicate that a rheumatic parent or child constituted a hazard per se to the nonrheumatic or quiescent members of the family group. Two different secondary attack rates were obtained. The rate for families in which one parent was rheumatic was double that for families in which

neither parent was rheumatic and four times as great in families in which both parents were rheumatic. These observations are apparently inconsistent with a hypothesis of contagion. They do, however, afford additional evidence that hereditary susceptibility underlies the familial incidence of rheumatic fever.

DISCUSSION

DR. HELEN B. TAUSSIG, Baltimore: Our studies in Baltimore fundamentally support those of the authors. My associates and I have found that there is a high familial incidence in rheumatic fever and there is evidence of a strong hereditary factor. We too have shown that its behavior is not that of an acute communicable disease. Its development is more like that of tuberculosis than like measles. We agree entirely that the incidence of rheumatic fever is higher in families in which one or both parents has had rheumatic fever than when neither parent has had the disease. On the other hand, I do not think this can be taken as evidence that the disease is primarily due to a hereditary predisposition and not an environmental factor. That belief rests on the assumption that chronic rheumatic fever is not contagious; we have no evidence to support that view. On the contrary, the fact that most people with rheumatic heart disease die of the disease leads to the belief that infection persists for a long time and may play an important part in the spread of the disease. It is noteworthy that after introduction of an acute case of rheumatic fever the secondary attack rate doubles and increases proportionately as much in the group in which the parents have not had rheumatic fever as in the group in which the disease is present in one or both parents. This, we believe, is evidence that this is an environmental factor. We have no indication whether the environmental factor is nutritional or exposure to damp and cold, but we do believe that there is an environmental factor as well as a hereditary one.

DR. JOHN R. PAUL, New Haven, Conn.: This discussion is concerned with the nature of rheumatic fever. More knowledge of this particular aspect of this disease is what we need. Dr. Wilson and her co-workers have used a difficult technic, but it is a method which holds some promise in the study of this and other diseases. It was used with success by Dr. Opie in tracing the spread of tuberculosis through families. The advantage, as the authors expressed it, which students of tuberculous families have over those who study rheumatic fever is that in tuberculosis there are many more diagnostic aids. One difficulty with rheumatic fever families is that of trying to discover what is really going on. The results in our family studies do not differ much from those that Dr. Wilson has shown, but our conclusions are, perhaps, not quite as definite. My associates and I believe that heredity plays an important, though not necessarily a dominant, part in determining the prevalence of this disease. We believe that there seems to be adequate evidence to show that the children of rheumatic parents acquire this disease with greater frequency than do the children of nonrheumatic parents. The degree to which hereditary influences prevail in rendering the host more or less susceptible to many infectious diseases is the question. Of course there must be strong environmental influences at work, such as climate, and poor living conditions. Another example of the effect of environment in rheumatic families is the manner in which upper respiratory infections precipitate an attack of rheumatic fever. Acute epidemics of rheumatic fever occur when an acute infection invades a "rheumatic family" just as they occur when such infections invade a convalescent home.

DR. JAMES F. RINEHART, San Francisco: The authors speak of a group in which the food was adequate and a group in which it was not adequate. I should like to ask to what extent a detailed analysis of nutrition was made. I am thinking of a possible deficiency in vitamin C.

DR. T. DUCKETT JONES, Boston: I should like to ask whether the authors have had any experience with offspring of rheumatic parents, either one or both, who have lived entirely away from the environment of the parents, even in different sections of the country, and especially where rheumatic fever is not common.

DR. MAY G. WILSON, New York: The data have not all been presented because of time limitations. We had 800 calendar years of activity, of which 25 per cent were simultaneous years,

that is multiple cases of activity during the same year. This is no more than might be expected by chance. The work reported by the Johns Hopkins group on the prefamilial and postfamilial attack rate is still a subject of debate between us. In these 112 families the children were not separated, but we know of families in our clinic in which children living apart from parents had rheumatic fever. I think data might be included on children who are adopted or sent out to other homes where there are non-rheumatic parents. I have asked those engaged in adoption work to look out for it. Such data would be significant. These homes have been under long observation of our social workers who were familiar with the food served to the children. Notes were made at each home visit as to the amount and balance of food, and particularly if vitamin C was inadequate.

Cultural Studies on Rheumatoid Arthritis and Rheumatic Fever

DRS. D. MURRAY ANGEVINE, SIDNEY ROTHBARD, and RUSSELL L. CECIL, New York: The patients with rheumatoid arthritis studied were those in the active stage of the disease, that is with pain and swelling of the joints and usually an increase in the sedimentation rate. The blood cultures were taken whenever possible in a dust-free, airfiltered room. Masks were worn by the operators during all procedures, and the transfers of cultures were made with rubber bulbs on the pipets. The aerobic clot method was used for most cultures. The principal medium used was dextrose phosphate broth. Repeated subcultures were made at intervals of five days for one month. Forty-nine of sixty-one (80 per cent) blood cultures made on fifty-eight patients yielded no growth. The following organisms were obtained from twelve of the cultures: Five showed a large gram-positive diplococcus (not identified), four *Staphylococcus albus* and the others an alpha prime streptococcus, *Staphylococcus aureus* and *B. subtilis* respectively. Additional cultures were made of synovial fluid and tissue, as well as subcutaneous nodules on similar medium enriched with horse blood. Twenty-two cultures of synovial fluid from twenty patients were sterile. Five of seven cultures of synovial tissue were sterile; *Micrococcus tetragenes* was grown in one instance and *Staphylococcus albus* in one. Five of nine subcutaneous nodules were sterile, three yielded *Staphylococcus albus* and one a gram-positive diplococcus. Special cultural studies were made according to the method of Klieneberger for the presence of a pleuropneumonia-like organism in the synovial fluid, synovial tissue or subcutaneous nodules from thirteen patients with rheumatoid arthritis. In no instance was such an organism recovered. The synovial fluid, tissue, or subcutaneous nodules from sixteen patients were inoculated on the chorio-allantoic membrane of the chick embryo, 185 eggs being inoculated and thirty-five subpassages made. No significant transmissible lesion was produced. Similar material was also instilled into the nares of young white mice (strain CF 1) under light ether anesthesia. Occasionally small areas of pneumonia developed after the first instillation. Thirteen of 127 mice injected in this manner developed small, patchy areas of pneumonia following the first instillation. Several passages, usually six, of normal and pneumonic lungs were made at intervals of from four to six days. In a few instances a transmissible pneumonia developed; however, this was so irregular and inconsistent that we feel it was probably caused by a mouse virus or pleuropneumonia-like organisms. Material from seven cases of rheumatoid arthritis was injected intravenously, intracerebrally, intraperitoneally or subcutaneously into mice. No significant lesions were produced, nor was any transmissible agent recovered. Irradiated mice were used in many instances; however, no difference was found between these and the non-irradiated mice in respect to the development of pneumonia.

Tissues or exudates from eleven clinical cases of rheumatic fever and from eleven cases at necropsy were studied. The following were cultured for pleuropneumonia-like organisms: synovial fluid four, pleural exudate three, pharyngeal washings four and heart valves with verrucous vegetations, pericardium or myocardium obtained at autopsy five. Similar material preserved by freezing from eleven of the cases was also cultured. In no instance were pleuropneumonia-like organisms recovered. The pleural fluid from one, and the synovial fluid from four

clinical cases, as well as tissue from three hearts obtained at autopsy, were inoculated onto the chorio-allantoic membrane and passed at intervals. No significant transmissible lesion was produced. Material from nine of the clinical cases and seven of the autopsies was instilled into the lungs of 145 mice and passages were made as previously described. In all, 486 mice were used. Sixty-seven mice were inoculated by other routes with material from two clinical cases and four autopsies. The results of these studies were similar to those described for rheumatoid arthritis.

Extensive cultural studies have been made in eighty-three cases of rheumatoid arthritis and twenty-two cases of rheumatic fever. No organism of significance has been consistently isolated.

DISCUSSION

DR. M. HENRY DAWSON, New York: Only one conclusion seems possible: if bacteria actually are present in the blood and joint tissues of patients suffering from rheumatoid arthritis they must exist in some form which cannot be detected by present day bacteriologic methods. Collier in Batavia, Java, has reported the occurrence of a spontaneous polyarthritis in rats. Cultures on the affected joints have been negative but the disease is readily transmitted from animal to animal. Findlay and his associates have described a similar disease in rats from which they have isolated a pleuropneumonia-like organism or "L form." I have had the opportunity of studying Collier's rats and have come to the conclusion that the disease is quite different from rheumatoid arthritis. Another interesting study has recently been reported by Collins on arthritis in swine. This disease is due to the organism *Erysipelothrix rhusiopathiae* and bears a closer relationship to the human disease. However, it is by no means clear that arthritis of swine bears any relationship to rheumatoid arthritis.

DR. HOMER F. SWIFT, New York: Dr. Brown and I made a preliminary report on the possible recovery of pleuropneumonia-like micro-organisms from rheumatic patients. We have now established that these micro-organisms probably originated from the mice inoculated with the exudates and have been unable to grow these germs directly from the exudates or tissues of patients with rheumatic fever. The technics have been so well developed that these negative results are significant. In animal inoculations Dr. Angevine and his co-workers used one strain of mice, of which about 10 per cent developed pneumonia. My associates and I employed another strain and obtained a much higher percentage of pneumonia, from which numerous pleuropneumonia-like micro-organisms were easily recovered when the pneumonic lung was rubbed over 30 per cent ascitic fluid agar and the plates were examined microscopically after from two to four days' incubation. In our studies mice inoculated with rheumatic exudates had a much higher proportion of pneumonia than did controls inoculated with nonrheumatic exudates. This suggests that possibly the rheumatic exudates contained aggrasin-like substances that made the pleuropneumonia-like micro-organisms carried by the mice in their upper respiratory tracts become more pathogenic; for, confirming Dr. Albert Sabin's studies, we have found that many of these mice carry in their conjunctivas these peculiar micro-organisms.

In reviewing the history of bacteriologic studies in rheumatism the question arises: Whence came the bacteria that have been reported as having been obtained? Outstanding among the various possible sources is the environment under which the cultures were made. Dr. Angevine's precautions in providing an atmosphere with little liability of contamination from air or other extraneous sources were important. In New York, at least, many positive cultures reported previously were made in Bellevue Hospital; and we know that in the old Bellevue Hospital it was difficult to find a good atmosphere, bacteriologically speaking. Before the advent of the automobile truck, horse manure was a prolific source of many streptococci in the air. Recently it has been shown that hemolytic streptococci are readily disseminated in the atmosphere of wards in which patients with scarlet fever or tonsillitis are treated.

Next arises the question of the significance of micro-organisms grown directly from blood cultures. When a tooth is pulled or tonsils are excised there is a certain period when bacteria, often

streptococci, actually circulate in the blood. In a patient with a sore throat it is conceivable that there is a period when streptococci break through the natural barriers into the blood stream. Obviously in the etiology of subacute bacterial endocarditis the agents infecting the heart valves must be bacteria carried originally by the blood. As already mentioned, when animals are employed to recover micro-organisms from a patient the difficulty always arises of determining whether the germs found are from the animal or patient. It should be indicated that the studies of Dr. Cecil and his collaborators have resulted in significant positive results. A few years ago when they were recovering streptococci from patients at Bellevue Hospital, he agreed to perform a blindfold test. The materials to be tested came from Presbyterian or Rockefeller Hospital and were sent to Dr. Cecil, who attempted to differentiate the rheumatic conditions in the patients from whom they came and made the correct diagnosis in many cases; but the differential feature was the agglutination by the serum of patients with rheumatoid arthritis of streptococci he had isolated from certain patients, and the absence of these agglutinins from the serum of patients with degenerative arthritis. Thus was discovered a test which many observers consider quite important. Lastly the discovery of the ability of pleuropneumonia-like micro-organisms to induce arthritis in mice and rats has led to a study of the beneficial action of gold salts in arthritis of these animals; and this type of experimental arthritis can be used to test the relative efficacy of various gold salts. I believe it has also been shown that other types of infectious arthritis in mice can be favorably influenced by these therapeutic agents. Thus, while the story is not finished, it still points to the value of experiments of this nature. Out of them progress is made toward an eventual solution of the mystery of arthritis.

DR. RUSSELL L. CECIL, New York: This is a negative report that seems to clear up a good many points. The studies of Drs. Nicholls and Stainsby were done at Bellevue Hospital; however, they were done in a sterilized room with great care and precaution. We were skeptical of these streptococci from the first. I think we were misled by the discovery of specific agglutinins in the patient's blood. Where did these streptococci come from? Dr. Nicholls and I often speculated about it when doubt was raised as to the accuracy of the work. The late Dr. Park thought the streptococci were actually in the blood but questioned their significance. We now think the pipets were the most likely source of contamination, rather than the air, since hemolytic streptococci are not common contaminants in air or on the skin. We think that, in spite of the cotton plugs in the sterile pipets, possibly some streptococci from the operator's mouth were blown through the pipets and introduced into the culture medium. This seems about as plausible an explanation as any. It would be difficult to set out deliberately and get 50 per cent contamination with streptococci in cultures. Bacilli of various kinds are common but it is unusual to get so many streptococci. The study of Dr. Angevine and Dr. Rothbard does not look pretentious but the number of animals used and the number of cultures made represent a great amount of work. As Dr. Swift said, this negative study means a really positive contribution to the subject. From my standpoint this report is in the nature of a retraction. I hope that a few years from now I shall not have to retract the retraction. I do not think that is likely.

DR. JOHN W. GRAY, Newark, N. J.: I am interested in the almost total lack of positive blood cultures in this report. One would normally expect a higher percentage from complicating acute upper respiratory infection alone, and if such cases were excluded from these studies the results might be of significance. Dr. Angevine and his collaborators made some cultures on my patients at the Hospital of St. Barnabas in Newark, and these patients had received sufficient treatment so that the disease became more or less quiescent. I have observed that positive cultures are seldom obtained during the summer months and that the largest number is found during the winter and spring months, when exacerbations of the disease following acute upper respiratory infections are most common. Whatever the cause of bacteremia may be, the presence of bacteria in the blood stream does not prove the microbic etiology of rheumatoid arthritis, nor does the absence of bacteria disprove it. I like Dr. Hench's conclusions regarding the infectious etiology of this disease when he

stated that as an investigator he must conclude that the evidence for infection, although impressive, is incomplete, but as a practicing physician he could not wait until evidence is complete and must commit himself, with reservations, to the microbic theory.

DR. R. H. FREYBERG, Ann Arbor, Mich.: About a year ago I became interested in the possible relationship between pleuropneumonia infection and the various rheumatic diseases, especially rheumatoid arthritis. With the assistance of Dr. Bauer and his associates, Dr. Dawson and others, I set about attempting to obtain cultures of pleuropneumonia-like organisms from synovial fluid, blood, subcutaneous nodules and the synovium itself of patients with rheumatoid arthritis primarily and of a few patients with rheumatic fever. All of the results have been entirely negative.

DR. J. ALBERT KEY, St. Louis: I had some negative results too in trying to obtain cultures of organisms from patients with rheumatoid arthritis, but changes which are practically identical with those found in rheumatoid arthritis can be produced in experimental animals by streptococci, although the polyarthritis which has been mentioned has not been produced. From the standpoint of the clinical course of the disease and from the standpoint of the pathologic changes that occurred in the tissues and also from the unexplained agglutination of streptococci which occurs in the blood of these patients I should regard this as an infectious disease. In spite of the sometimes positive, sometimes negative observations, statements and retractions, one may be prepared some day for Dr. Cecil to retract his retractions.

DR. CHARLES W. WAINWRIGHT, Baltimore: I should like to ask the authors concerning the status of the agglutination reaction in their cases of rheumatoid arthritis because this has been to my mind an important contribution in the study of this disease, provided they represent true agglutinins. There are many features about the reaction which point to true agglutinins and, on the other hand, features which indicate that it might be some curious physical-chemical phenomenon peculiar to this disease.

DR. T. DUCKETT JONES, Boston: During the past three or four years my associates and I isolated, according to the technic which Dr. Angevine described, a virus from the heart tissues of several patients with fatal rheumatic fever. The changes developing in the lungs of mice were interesting. The blood of the rheumatic fever patients neutralized this virus. The following year, however, we had less luck in isolating a virus from patients with fatal rheumatic fever. We tried not only cardiac but pulmonary tissues. To summarize, it soon became evident that the virus which was isolated was similar to the virus which can be isolated from patients with influenza. What this means we do not yet know. There are many other factors that come into play. The pleuropneumonia-like organisms and the question of mice viruses also enter the picture. We have isolated some which are similar to the noninfluenzal viruses recently described by Horsfall. Others isolated from stock mice behave much like the influenzal viruses. We now feel that we have isolated an influenza-like virus from rheumatic fever patients and from the respiratory tract rather than the heart. Whether it has any direct bearing on rheumatic fever it is impossible to say, but further studies of the presence of neutralizing antibodies in rheumatic fever patients may prove to be interesting.

DR. D. MURRAY ANGEVINE, New York: I should like to say something about the recovery of micro-organisms from the blood stream. One can take a blood culture on a pig at almost any time during twenty-four hours and recover organisms from the blood stream. Blood cultures can be taken from patients after a meal, and frequently organisms are recovered. If the blood of normal rabbits is repeatedly cultured, organisms may be recovered in perhaps 5 per cent of instances. In addition to the intrapulmonary route, we have injected mice intravenously, intracerebrally, intraperitoneally and into the foot pad. Dr. McEwen took cultures of the blood of various patients over a period of two years. It is of interest that in one year 20 per cent of the cultures were positive, whereas in the other year the incidence was much lower. I did not intend to mention the streptococcus agglutination reaction for we are still in a state of flux concerning it. When we began our work, a good many positive tests

were obtained. However, as we have continued, there has been considerable variation in the results. During a period of four years, out of about 300 agglutination tests on definite cases of rheumatoid arthritis, our percentage of positives would be about 45. This is approximately the same figure as that reported by Dr. Bauer. Dr. Key suggests that we are getting away from the infectious theory of this disease. I may say that we have been continuously working along this line in animals. Two years ago in a report before this society, we showed pictures of what we thought were rather typical of the pathologic changes usually seen in rheumatoid arthritis. They showed lymph follicles produced by streptococci. So far we have not been able to obtain these lymph follicles in the synovia of any other animal except the rabbit.

Metabolism of Cartilage (Bovine) With Particular Reference to the Effects of Aging

DRS. OTTO ROSENTHAL, MORRIS A. BOWIE, and GEORGE WAGONER, Philadelphia: Cellular and metabolic studies have been made on bovine articular cartilage of varying ages. The cartilage from the older animals showed degenerative changes characteristic of hypertrophic arthritis. Microscopic examination and measurements of paraffin embedded slices of cartilage showed (a) the number of cells per cubic millimeter of tissue (cell content) declined with advancing age, and (b) the mean values of nuclear volume remained constant throughout the age groups.

The metabolic activity of surviving cartilage slices was determined by the method of Warburg. This activity was expressed as a ratio of metabolic rate to cell content. Glycolytic activity and the activity of the dehydrogenatic and oxygen-activating components of respiration were determined for cartilage of various ages. (a) Glycolytic activity remained essentially the same in all age groups. (b) Dehydrogenatic activity was determined from the oxygen uptake in the presence of methylene blue. It likewise remained essentially unaltered. The dye-stimulated respiration was accelerated by the addition of dextrose, succinate, lactate and pyruvate. This acceleration indicated that the cartilage cell is endowed with enzymes for the dehydrogenation of these four metabolites. No detailed analysis was made of the main part of the dye-stimulated respiration which is based on utilization of tissue metabolites. The respiratory quotient (0.85) of these processes suggested oxidation of protein and fat. (c) The oxygen-activating component of respiration was estimated by measuring the spontaneous oxygen consumption of cartilage. The activity of this component declined 65 per cent from infancy to old age. This decline coincided and progressed with appearance and extension of the degenerative changes in cartilage.

Gradual failure of spontaneous respiration with aging hinders the use of the dehydrogenatic processes which are important in cellular anabolism. When to this is added the diminution of cell content, it must follow that the intrinsic integrity of aged articular cartilage is materially weakened.

DISCUSSION

DR. KARL MEYER, New York: Cartilage seems to be especially suited for a study like this because apparently its metabolism is fairly constant over the period of time in which one is working, and, second, because it is a relatively simple tissue in which one can study not only the energy production but also for what chemical processes the energy is used. To connect the energy metabolism with the production of chondroitin, sulfuric acid seems to be possible since there are methods available to determine the amount of hexosamine and from that figure calculate the amount of chondroitin sulfuric acid in cartilage. It would further be interesting to study the production of glycuronic acid in cartilage. Is the failure of oxidative processes which the authors demonstrated connected with a failure to oxidize dextrose or a dextrose equivalent into glycuronic acid? How does this total metabolism of cartilage change with age? It is said that apparently the total volume of the cartilage is not changed with age, though some of its components are. This may mean that the aging cells must produce some components other than the young ones. Apparently chondroitin sulfuric acid is replaced by connective tissue or other fibrous tissue for the pro-

duction of which not so much energy may be required. The production of this fibrous tissue may require quite a different type of metabolic activity from that of young cartilage.

DR. MARIAN W. ROPES: The onset of degenerative joint disease in the cartilage makes study of the alterations of metabolism with age of special significance. The value of this work has been greatly increased by correlating the analytic results with the number of cells. The low rates of metabolism are in accord with the avascular nature of articular cartilage and its limited reparative ability. However, while such work is essential, it is also extremely difficult to control and interpret. Great caution is necessary in drawing conclusions to avoid misleading results which would tend to bring essential studies of this type into disrepute. The conflicting results in this study and that of Bywaters make further work necessary. Apparently some of the determinations of Bywaters were on young cartilage, so that the differences cannot be explained entirely on age. The values of oxygen consumption are in such a low range that errors are magnified and all factors in the method become significant. I should like to ask how thick the slices were, whether one could be sure that oxygen was reaching all cells; whether control slices, heated to kill the cells, were used; whether the sterility was carefully checked, and how long the experimental runs lasted. Also I should like to know whether the slices were perpendicular to the surface as would be essential for comparable distribution of cells, and whether consecutive slices were used for metabolic experiments and microscopic study, both for number of cells and for degenerative changes, for especially in cartilage with degenerative changes there are great variations from one area to another. In any case it would seem almost impossible to rule out the errors from the clustering of cells that is known to occur. Was the change in specific gravity of the matrix considered in estimating the cell mass? If cartilage cells are larger in old age, as has been suggested though not proved, the calculation of cell mass would be incorrect and much if not all of the change in oxygen consumption with age could be explained. The magnitude of glycolysis in proportion to oxygen consumption and the predominance of dehydrogenase activity over the oxygen activating system have been well shown by Dr. Bowie's work. Whether the low respiratory activity decreases with age seems less conclusively proved. Its significance in terms of energy is changed only from 170 to 135 per cent from youth to age. Finally, whatever metabolic differences exist between young and old cartilage, there is no evidence that they are the cause rather than the effect of degenerative changes.

DR. DAVID H. KLING, Los Angeles: Dr. Bywaters has proved that articular cartilage is a tissue of low metabolism. The objection of the authors that he worked with old cartilage of reduced metabolism does not appear to invalidate his results because he conducted a comparative study of metabolism of synovial membrane and cartilage from the same joint. He found that the oxygen consumption per cell of cartilage was less than one-hundredth of that of synovial cells and, although glycolysis was higher, it amounted to only one-eighth that of synovial membrane from the same joint. Articular cartilage is an avascular tissue. Nutrition is of less importance for maintenance of integrity of avascular tissues than protection. It was experimentally proved that, if articular cartilage is exposed to drying or to pH values below 7, erosion and degeneration take place. Jones has demonstrated that friction due to movement of joints without lubrication results in heating and rapid deterioration of articular cartilage. This evidence indicates that the most important factor for the maintenance of proper lubrication and protection of the articular cartilage is the synovial fluid. Pathologic changes of this fluid, perhaps also disturbances of the blood supply of the synovial tissue with increased age, appear to be more significant than deficiencies of nutrition for development of degenerative changes of articular cartilage.

DR. OTTO ROSENTHAL, Philadelphia: The presence of glycolytic and dehydrogenatic enzymes in articular cartilage was shown by Bywaters when he found that cartilage split dextrose to lactic acid and consumed oxygen after the addition of methylene blue. The nature of the dehydrogenatic processes was not demonstrated by Bywaters. Dehydrogenases without oxygen-

activating enzymes are of little value for the function of a cell. A cartilage cell endowed solely with glycolytic power could hardly produce the variety of substances which constitute its matrix. Therefore it seemed to us of interest when we found that young cartilage has a definite respiratory power and when it was possible to elucidate to some extent the nature of the dehydrogenatic processes. Qualitatively the metabolism of cartilage does not differ as greatly from that of other tissues as was assumed. A detailed study of the oxidative enzymes was not attempted because it would have required the use of tissue extracts. We restricted our studies to the reactions of surviving tissue. The presence of catalase, therefore, was not investigated. Indophenol oxidase is apparently present in cartilage, since paraphenylene-diamine is oxidized by the slices. As Dr. Meyer pointed out, it would be of importance to find out what the cartilage cell does with the energy it obtains from either glycolysis or respiration. To solve this problem we must study anabolism and catabolism of cartilage constituents such as chondroitin sulfuric acid. It might be worth mentioning that cartilage splits one constituent of this acid, namely galactose, and that the enzyme involved is different from the glycolytic enzyme. The mechanism of this enzymatic process remains to be solved. Since the respiration of cartilage is constant over a period of from three to five hours, it is not difficult to obtain reliable readings. The thickness of the slices was around 0.5 mm. in all the ages studied, i. e. the slices were sufficiently thin to guarantee optimal oxygen supply. Oxygen consumption as well as glycolysis and dehydrogenation disappear completely after immersing the vessel with the slices for six minutes in boiling water. I think we can deny with certainty the question as to whether a miscalculation of the cell content could have accounted for the respiratory decline in the aging cells. Our assumption that the cellular mass is proportional to the cell content of the fixed tissue is tentative. An estimate of the shrinkage of the tissue in the course of the embedding procedure and a separate determination of the specific gravity of the cells and of the matrix in the age groups were not possible. But we believe that the magnitude of the cellular activity was obtained without applying these corrections. Even if we disregard completely these data, the respiratory failure with aging remains a fact because the ratio of respiration to glycolysis decreases with advancing age to the same extent as the ratio of respiration to cell content. With regard to the cause of arthritis, we never claimed that the respiratory failure in aging cartilage is the only cause of degenerative arthritis, but we believe that it is an intrinsic factor of aging. So far I think it has been of some advantage to replace one vague term by a definite process.

Latent Brucellosis: Its Importance in Association With Joint, Muscle and Nerve Pain

DRS. WARD DARLEY, and R. W. GORDON, Denver: If the intradermal tests with Brucella antigen is a reliable index to Brucella sensitization, the use of the test in a large series of patients should be of value in indicating the possible importance of Brucella sensitivity in certain chronic illnesses, particularly those in which neuroskeletal-muscular complaints are prominent. Of 1,027 "ailing" and 360 "well" individuals tested, 15.48 and 8.88 per cent respectively gave positive reactions. Of 159 positive reactors only fifty-four were found in whom a positive skin test was the sole objective finding and in whom there appeared to be no complicating neurosis. In this group neuroskeletal-muscular complaints stood second in incidence (62 per cent). Of 124 patients with hypertrophic arthritis, 13.7 per cent gave positive reactions. Eighteen per cent of eighty-nine patients with infectious arthritis gave positive reactions. Symptom comparison of the skin negative cases in this group with the fifty-four uncomplicated reactors, except for the constancy of joint complaints, revealed in general a lower incidence for all the symptoms tabulated.

Of 301 patients with personality determined disorders 26.5 per cent were positive reactors, and of 159 reactors eighty, or 45 per cent, had maladjustment problems. Fifty-eight Brucella sensitive patients were found in whom the only other observations were functional in nature. Symptom comparison of this group with the fifty-four uncomplicated reactors revealed little difference

except a much higher incidence of nervous and emotional complaints. One hundred nonreactor cases of personality maladjustment were also studied (as a control group) and it was found that the incidence of neuroskeletal-muscular complaints was essentially the same as in both the fifty-four uncomplicated reactors and in the group of fifty-eight cases.

In general we conclude, then, that *Brucella* sensitization is commonly found in patients with subjective neuroskeletal-muscular complaints whether they have associated personality problems or not. It would appear to us that each individual skin positive case should be carefully evaluated as to *Brucella* immunity or activity and as to the presence of personality determined disorders before mapping out therapeutic procedures.

DISCUSSION

DR. EPHRAIM GOLDFAIN, Oklahoma City: If *Brucella* causes psychoneurotic complications, then naturally the reverse is true. Psychoneurotic persons when seen by physicians should be investigated for latent brucellosis. Specific treatment of these psychoneurotic patients should be carried on concomitantly with other treatment measures, even if it is only an aggravating factor rather than a true cause of the individual patient's symptom complex. Briefly I wish to set forth observations noted as a result of routine testing by means of agglutination, opsonocytophagocytic, and cutaneous tests all cases seen in which arthritic or rheumatic symptoms were present. Where objective arthritic observations are present and other causes which explain the presence of the arthritis are lacking, except positive agglutination, opsonic index and cutaneous tests, there will quite often present itself to the examining physician the following outstanding subjective and objective observations: 1. Periarticular swellings, often resembling a typical case of atrophic arthritis. 2. Cold, clammy skin of hands. 3. Lack of response to removal of apparent foci of infection. 4. Often lack of response to other therapeutic measures. 5. Presence on x-ray examination of a lack of bony tissue involvement yet the presence of swellings typical of atrophic arthritis. 6. Absence of marked secondary anemia. 7. Absence of streptococcus antibodies. 8. Moderately active red cell sedimentation test. 9. Quite regularly a high titer of agglutination for the *Brucella* organism as well as a high opsonic index test and a strongly positive persistent *Brucella* cutaneous test. 10. Neurasthenia.

DR. WILLIAM J. KERR, San Francisco: In recent years I have seen some of the more chronic or protracted conditions that may occur in connection with brucellosis. In general one sees a number of complications or later involvements similar to those seen in typhoid. I have seen osteomyelitis of the spine and osteitis of the bone of the face and the floor of the antrum, and a number of others have been observed and described. Drs. Darley and Gordon have brought up a question which has been in my mind for a long time. How can one differentiate the group of symptoms that these patients complain of from those seen in the neurotic or psychoneurotic patient or in the psychotic patient? I think the authors have shown that most of the symptoms are exactly those seen in persons who have been ill for a long time with any chronic disease. It is this same group of symptoms which are difficult to differentiate from the symptoms of toxic goiter. Aside from the greater incidence of fever in this group there is some suggestion that they may have chronic or prolonged effects of brucellosis, and there was little else that seemed of great significance. However, those who were chosen for the group of psychoneuroses or insanity states show a preponderance of symptoms in favor of anxiety states. I have seen quite a number of patients who were known to have had brucellosis and who have been observed for a period of several years. It seemed to me that in them the most difficult symptoms to control were the symptoms which have been described. I believe that there is no proof as yet that they are due to the infection itself or to the lasting effects of some hidden focus of some other infection of this general type, but they appear to belong to the symptoms seen in any chronic invalid. If one undertakes to treat these symptoms by vaccines, the only effect will be by suggestion. This may be justifiable, but I think it is bad medical practice, particularly since it tends to mislead one as to values in treatment.

DR. D. MURRAY ANGEVINE, New York: We have taken a good many agglutination tests on serum as well as a good many cutaneous tests both for brucellosis and for abortus infection. In no patient from the Arthritis Clinic of the New York Hospital have we found any indication that brucellosis is a serious problem in relation to arthritis in New York City.

DR. W. PAUL HOLBROOK, Tucson, Ariz.: The authors have presented a series of control cases and have proved that the presence of a previous brucellosis as evidenced by a positive cutaneous test has no more to do with the etiology or joint manifestations than a positive tuberculin test. In my part of the Southwest the finding of rheumatoid arthritis with brucellosis is certainly uncommon. I have always doubted that brucellosis can produce a typical rheumatoid arthritis. It may be that it does occasionally.

DR. R. H. FREYBERG, Ann Arbor, Mich.: In Ann Arbor we studied twenty-five patients who had typical rheumatoid arthritis and twenty-five other patients who came to the hospital complaining of symptoms of a rheumatic nature but whose disease was not characteristic of any common type of arthritis. We studied these two groups of patients in the same way by doing blood cultures for *Brucella*, by doing cutaneous tests and opsonocytophagic indexes, taking careful histories and making physical examinations. None of the patients in the first group had any evidence that we could consider indicated or allowed a diagnosis of brucellosis. Three persons in the second group had what we considered to be definite evidence of brucellosis; and six others had "possible brucellosis." From this study we concluded that joint symptoms frequently exist with brucellosis: acute arthritis may occur, but chronic joint inflammation seldom if ever results from brucellosis.

DR. E. STERLING NICHOL, Miami, Fla.: I would offer a word of caution about assuming too definitely that the neuromuscular complaints in chronic brucellosis are due to psychoneurosis rather than to the infection. Individuals afflicted with chronic brucellosis do poorly in the climate of southern Florida. After seeing a number of so-called psychoneurotic patients experience gross exaggeration of their neuromuscular complaints after migration to the latitude of southern Florida, I am of the opinion that an occult *Brucella* infection may account for some of these complaints, a view which has been substantiated in some instances by clinical investigation.

DR. WARD DARLEY, Denver: The biggest questions that confront most of us (as far as *Brucella* sensitization is concerned) are decisions as to the cause of the patient's symptoms and the selection of cases for treatment. I feel that one still has to depend for the most part on clinical judgment, but it is only natural that one should turn to the laboratory for help. Given a positive cutaneous test, one should decide whether the patient is immune and thus from the practical standpoint whether he is still actively infected. I am afraid that unless the various tests are properly understood they will only add to the confusion already so evident in the study of brucellosis. The agglutination reaction is usually negative in the skin positive cases. There is no agreement among investigators as to how strong an agglutination one must have before infection is considered active. Some investigators consider titrations as low as 1:10 as significant. Most investigators require titrations of 1:80 or more before considering a given case as one of active infection. There were about twenty of our patients who had agglutinations of 1:50 or above. The opsonic phagocytic index theoretically should be of value. It is a complicated procedure and its interpretation is a matter of controversy, even if done correctly. The complement fixation reaction may offer a possible solution to this problem. To date, reports in the literature are few as far as its application to brucellosis is concerned. The sedimentation rate is of no help. I do not want to be misunderstood regarding the relationship between brucellosis and psychoneurosis. I do not think that latent brucellosis can be used as an explanation for psychoneurosis. It is possible that *Brucella* sensitization may render an individual more susceptible to personality maladjustment. We do not feel that it can be a primary cause. In our experience psychotherapy, in these instances, is more important than specific anti-*Brucella* therapy.

(To be continued)

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore 10:673-770 (Oct.) 1940

- *Vitamin K in Hemorrhagic Diseases of Infants and Children. I. N. Kugelmass, New York.—p. 673.
- Actinomycosis: Review with Detailed Clinical and Autopsy Reports of One Case Each of Intestinal and Ovarian Forms. L. S. Auster, New York.—p. 688.
- *Primary Splenic Neoplasms. S. A. Goldberg, Newark, N. J.—p. 700.
- Stromal Tumors of Choroid Plexus. A. F. Liber and J. R. Lisa, New York.—p. 710.
- Unusual Manifestations and Pathology of Congenital Syphilis. K. E. Landé, Hagerstown, Md.—p. 736.
- Influence of Cobalt on Iron Transportation and Storage: Chemical and Histologic Study. K. Kato and Vivian Iob, Chicago.—p. 751.

Vitamin K in Hemorrhagic Diseases of Children.—Kugelmass points out that the wide range of fluctuation (a deficiency of as much as 80 per cent with no hemorrhagic manifestations and an excess up to 300 per cent without thrombotic phenomena) indicates the instability of the clotting mechanism when disease affects its components. Several hundred blood clotting determinations have led to the conclusion that prothrombin is not a determining factor in purpura, hemophilia or scurvy of infancy and childhood except in rare hemorrhagic disturbances (hemorrhagic disorders of the newborn, neonatal icterus gravis, hepatic pseudothrombophilia and hereditary pseudothrombophilia). They may be related to intestinal disorders preventing biliary absorption of vitamin K or to hepatic or bone marrow dysfunction interfering with the synthesis and subsequent liberation of prothrombin into the blood. Therefore vitamin K may raise blood prothrombin if intestinal absorption and reticulo-endothelial synthesis are adequate. Each case of neonatal hemorrhagic disease differs in its cause and course but the bleeding is invariably due to prothrombin deficiency. Nine of ten such cases showed marked depression in the prothrombin content of the blood with a corresponding lowering in the clotting time. Since the determining factor was consistently a decreased blood prothrombin the condition was designated acute hypoprothrombinemia. The mild form of the disease is undoubtedly self limited, as two of the ten cases were discovered only during routine clotting time determinations. Severe cases respond poorly to all forms of therapy in spite of early diagnosis. These have been associated with prenatal transmission of the disease indicated by the lowered prothrombin content of the expectant mother's blood. Vitamin K appears of equal value with blood transfusion in mild cases, the one forming prothrombin and the other providing it. But mild cases offer no final criteria because coexisting hematogenic jaundice may diminish its absorption and utilization and thus interfere with its synthesis. That vitamin K raises the prothrombin levels is no index of its efficacy in the presence of hemorrhagic disease characterized by injury to the reticulo-endothelial system. Therapy should not be limited to a precursor of prothrombin when the active substance, blood, is available. The routine use of vitamin K to protect the newborn from possible hemorrhagic disease is not indicated as there is ample prothrombin for clotting shed blood. Further abnormally high prothrombin levels cannot prevent blood from oozing through a damaged vascular system unless the entire circulation is clotted. The contention that the prevention of neonatal hemorrhagic diseases will diminish intracranial hemorrhage is only partially true, as the former is a disease of the blood and the latter a result of trauma to the vascular system. A normal blood coagulability does not preclude vascular injury and vice versa. The two diseases are more often mutually

exclusive than coexistent. In icterus gravis neonatorum the bleeding tendency depends more on the extent of damage to the liver parenchyma than on the degree of jaundice. The low blood prothrombin is probably a secondary manifestation of progressive hepatic dysfunction which interferes with the synthesis of prothrombin. A case of obstructive jaundice with hemorrhagic manifestations cleared on the second day following 1 cc. of vitamin K in oil given in conjunction with bile acids three times a day. The blood picture was within normal limits after a week of severe jaundice. In hepatic pseudothrombophilia accompanying infectious invasions or chemical poisoning the bleeding is due to a decreased production of prothrombin or fibrinogen or both in the liver with a resultant diminution in their concentration in the blood characterized by a markedly prolonged clotting time. A case of infective jaundice with hemorrhagic manifestations responded favorably to vitamin K. Marked hemorrhagic episodes in this condition are primarily determined by the qualitative defect in platelets, and therefore vitamin K is not indicated unless there is a coincident decrease in prothrombin during mild interim attacks.

Primary Splenic Neoplasms.—Goldberg reports one hemangioma cavernosum removed surgically as spleen and three primary neoplasms of the spleen: a solitary hemangioma cavernosum, a solitary microcystic lymphangioma and a multiple macrocystic lymphangioma. The three primary cases were encountered among 575 necropsies, in which there also were ten secondary malignant neoplasms. These ten neoplasms were obtained from ninety-eight cases of carcinoma, giving a greater incidence (9.8 per cent) of splenic metastases than is recorded in the literature. The case of cavernous hemangioma of the spleen consisted of a solitary nodule in an otherwise normal spleen and was apparently an early neoplasm. The cases reported in the literature are mostly large cystic hemangiomas. The microcystic lymphangioma consisted of a solitary nodule 8 mm. in diameter, apparently an early growth in an otherwise normal spleen. The stroma was quite cellular in places, containing lymphocytes, endothelial cells and budding vessels, and therefore the lymphangioma belongs in the category of a neoplasm. The macrocystic lymphangioma was composed largely of lymph spaces separated from one another by a fibrous and cellular stroma, and a few blood vessels. These last two tumors appear to be real neoplasms rather than simple telangiectatic areas, since the lymph spaces are separated by a cellular stroma containing budding vessels. They conform to Ewing's description of cystic and cavernous lymphangioma. The bulky hemangioma cavernosum removed from the region of the spleen is considered spleen. The light area in the center of this tumor was composed mostly of mucoid connective tissue and possibly was a stage in the formation of fibroma said to develop from a cavernous hemangioma.

American Journal of Physiology, Baltimore 130:613-814 (Oct.) 1940. Partial Index

- Pressor Response to Adrenalin in Course of Traumatic Shock. A. M. Freedman and H. Kabat, Minneapolis.—p. 620.
- Measurement of Venous Pressure in Man Eliminating the Hydrostatic Factor. J. P. Holt, Chicago.—p. 635.
- Reciprocal Innervation in Small Intestine. R. Hodes, Boston.—p. 642.
- *Dark Adaptation and Experimental Human Vitamin A Deficiency. S. Hecht and J. Mandelbaum, New York.—p. 651.
- Growth and Development of Six Generations of Thymectomized Albino Rats. A. Segaloff and W. O. Nelson, Detroit.—p. 671.
- Changes in Respiration on Inflation and Deflation of Chest. J. K. W. Ferguson, Toronto.—p. 675.
- Temperature Regulation in Chronic Cervical Cats. G. Clark, Chicago.—p. 712.
- Hemolytic Action of Chyle. L. W. Freeman and V. Johnson, Chicago.—p. 723.
- Effect of Climate on Volumes of Blood and of Tissue Fluid in Man. W. H. Forbes, D. B. Dill and F. G. Hall.—p. 739.
- Action of Heparin, Serum Albumin (Crystalline) and Salmine on Blood Clotting Mechanisms (in Vitro). J. H. Ferguson, Ann Arbor, Mich.—p. 759.
- Rate of Respiratory Adjustment to Postural Change. M. H. Soley and N. W. Shock, San Francisco.—p. 771.
- Effect of Oxygen Tension of Inspired Air on Respiratory Response of Normal Subjects to Carbon Dioxide. N. W. Shock and M. H. Soley, San Francisco.—p. 777.

Dark Adaptation and Vitamin A Deficiency.—Hecht and Mandelbaum determined the dark adaptation of seventeen men from 21 to 30 years of age before, during and after their stay on a vitamin A deficient diet. The data show that cone and

a favorable medium which contains peptone-like substances and that only a relatively low concentration of the drug is obtained by systemic administration of sulfanilamide, it is obvious why such administration is not effective.

Sulfanilamide and Internal Fixation for Compound Fractures.—Campbell and Smith studied the prophylactic action of sulfanilamide on infection in fifty-four compound fractures including those with internal fixation. The results were sufficiently favorable to warrant further use of the drug. The cases of fractures are divided into three groups: fresh compound fractures, old compound fractures with a previous infection, and compound fractures with an active draining infection. In a portion of the first series, from 15 to 20 Gm. of sulfanilamide crystals was placed directly into the compound wound and the wound was closed without drainage. After twenty-four hours sulfanilamide was continued by mouth, from 15 to 20 grains (1 to 1.3 Gm.) every four hours. Of the ten cases of the thirty-five in the first group in which infection developed, cultures revealed *Staphylococcus aureus* in five, Welch's bacillus in three, *Streptococcus haemolyticus* in one and the organism was not recorded in one. These figures would suggest that sulfanilamide had a less favorable prophylactic action on staphylococcal and Welch's bacillus than on streptococcal infections. Sulfanilamide or azosulfamide was administered as a routine to the seven patients of the second group; the average dose was 8 Gm. of the former or 10 Gm. of the latter for from twenty-four to forty-eight hours prior to the operation and for from three to seven days after operation until there was no longer any danger of infection. No infections ensued in these seven cases. In the remaining twelve surgery was performed in the face of an active draining infection. The dosage of sulfanilamide, or azosulfamide, was similar to that administered in the presence of compound fractures with latent infections. Bacteriologic studies showed *Staphylococcus aureus* in three, *Staphylococcus haemolyticus* in two, *Streptococcus haemolyticus* in two, and the observations in five were not recorded. There have been no infections following internal fixation in ten; union has occurred in ten and it is too early for prognostication in two. In a number of the operative cases draining sinuses persisted for several weeks to months but the wounds ultimately closed and the bones united. In no case was it necessary to remove any of the plates, screws, nails or wires. The results in this group were the most striking of the entire series. Comparison with comparable controls shows better anatomic and functional results following internal fixation in conjunction with sulfanilamide than when internal fixation and sulfanilamide are not employed. The authors conclude that the present impression of sulfanilamide is favorable but that more extensive investigation must be carried out with sulfanilamide and other chemotherapeutic agents before accurate evaluation will be possible.

Treatment of Cerebral Palsies.—Phelps points out that, according to surveys in various parts of the country begun a few years ago, it may be assumed that there are at least 150,000 cases of cerebral palsy in the United States. A survey of children from 2 to 16 years of age in Maryland showed a yearly occurrence of seven cerebral palsy births per hundred thousand of population. In other parts of the country surveyed this ratio is fairly constant. The percentage of cases found in the Negro race is much lower than in the white race. A study to determine what percentage of patients had sufficiently high mental status to become worthwhile members of society showed that, if the physical difficulties could be alleviated, 68.8 per cent had good mental ability and that 72 per cent have a mild or moderate handicap. The problem of the cerebral palsies includes a large number of patients who would justify the time and expense of treatment. Severity of involvement is not always a contra-indication to treatment. Treatment depends on a careful diagnosis of the particular kind of cerebral palsy: spastic, athetoid or ataxic. A complete muscle examination should be made in all cases. No operation should be performed on a spastic muscle without examination, as the condition of the antagonists is often the deciding factor in determining the procedure. In conservative treatment the flaccid and weak muscles must be protected from the weakening effect of undue stretching, and the spastic

muscles from the strengthening effect of the stretch reflex. With selective massage, careful exercise, appropriate splinting and protection a great change in muscle balance may be attained. The amount of surgery apparently necessary at first will be greatly diminished. In athetosis a muscle examination will demonstrate those muscles which move involuntarily and those which do not. Athetosis seems better conceived as an involuntary attempt to move a joint in a certain way than as an involuntary stimulation of any individual muscle. Therefore surgical intervention on the muscles, nerves or tendons has little effect. Joint stabilizations are exceedingly difficult. The discomfort of the patient following the operation is marked and there is much difficulty with pressure sores. In general, operative procedures are unsuccessful. In severe cases Putnam's procedure is helpful; it quiets the athetosis but does not increase function. The further use of curare should be watched with interest. Carefully graded and prolonged relaxation beginning with the least athetoid parts of the body and extended to the more athetoid extremities combined with motion from the relaxed position eventually brings satisfactory results. The treatment of ataxia is that of training the voluntary motor centers to take over the function of the damaged balance mechanism. It can be compared to the learning of any other skill, such as playing the piano, which in time is carried out almost without thought. Thus, with sufficient practice the skill of balance and directional control can be learned until eventually it becomes habitual. The ideal place to train these patients is in a school or institution where their physical and educational needs are met until such time as bad habits can be broken and rehabilitation carried out. There is great danger of old habits returning at home, because they are so closely bound up with the home environment. After discharge from the institution, treatment should be continued individually at least three times a week to insure fixation of progress. It should be decreased gradually over a period of years as skills are taught which take the place of exercises. Obtainable results lie in three fields—use of the legs, use of the arms and speech. Speech disorders are likewise spastic, athetoid or ataxic, and the same principles of treatment apply. Satisfactory results, judged by the standards of other crippling conditions, are obtained when care and treatment are sufficiently intensive.

Journal of Nutrition, Philadelphia

20:305-412 (Oct.) 1940

- Intravenous Administration of Crystalline Amino Acids to Infants. A. T. Shohl and K. D. Blackfan, Boston.—p. 305.
Fat as Factor in Healing of Rickets with Vitamin D. A. Knudson and R. J. Floody, Albany, N. Y.—p. 317.
Determination of Ascorbic Acid in Evaporated Milk, Powdered Milk and Powdered Milk Products. W. W. Woessner, C. A. Elvehjem and H. Schuette, Madison, Wis.—p. 327.
Modification of Line Test Applicable to Chicken Vitamin D Assay. E. W. McChesney and E. Homburger, Rensselaer, N. Y.—p. 339.
Composition of Gains Made by Rats on Diets Promoting Different Rates of Gain. Marjorie Pickens, W. E. Anderson and A. H. Smith, New Haven, Conn.—p. 351.
Influence of Fat on Calcium and Phosphorus Metabolism. J. H. Jones, Philadelphia.—p. 367.
Influence of Dietary Riboflavin on Content of This Vitamin in Chicken Tissue. A. Z. Hodson, Ithaca, N. Y.—p. 377.
Comparative Assimilation of Fluorine by Growing Rats During Continuous and Intermittent Dosage. Margaret Lawrenz, H. H. Mitchell and W. A. Ruth, Urbana, Ill.—p. 383.
Availability to White Rats of Phosphorus in Soybean and Red Clover Hays, Dorothy E. Williams, Florence L. MacLeod and Elsie Morrell, Knoxville, Tenn.—p. 391.
Prevention and Cure of Nutritional Muscular Dystrophy in Rabbit by Alpha-Tocopherol in Absence of Water-Soluble Factor. C. G. Mackenzie, M. D. Levine and E. V. McCollum, Baltimore.—p. 399.

Journal of Pharmacology & Exper. Therap., Baltimore

70:165-244 (Oct.) 1940. Partial Index

- Actions of Methyl-Atropine Nitrate (Eumydrin). J. D. P. Graham and S. Lazarus, Glasgow, Scotland.—p. 165.
Changes in Blood Pigments Associated with Prolonged Administration of Large Doses of Acetanilid and Related Compounds. P. K. Smith, New Haven, Conn.—p. 171.
Effects of Intravenous and Intraperitoneal Introduction of Polyvinyl Alcohol Solutions on Blood. W. C. Hueper, J. W. Landsberg and L. C. Eskridge, New York.—p. 201.
Toxicity, Trepanemicidal Activity and Potential Therapeutic Utility of Substituted Phenylarsenoxides. H. Eagle, Baltimore; G. O. Doak; R. B. Hogan, Baltimore, and H. G. Steinman.—p. 211.
Comparison of Digoxin with K-Strophanthosid. J. M. Walker, Oxford, England.—p. 239.

Kentucky Medical Journal, Bowling Green

38:423-470 (Oct.) 1940

- Aims and Aspirations. A. Bell, Hopkinsville.—p. 424.
Lung Abscess. A. E. Grimes, Lexington.—p. 430.
Evolution of Our Knowledge of Tuberculosis. O. O. Miller, Louisville.—p. 434.
Management of Patients with Acute Myocardial Infarction. T. R. Harrison, Nashville, Tenn.—p. 442.
Intestinal Obstruction. B. E. Caywood, Danville.—p. 446.
Pathology of Primary Tuberculosis. B. L. Brock, Louisville.—p. 450.
Clinical Symptoms of Tuberculosis in Children. W. W. Nicholson, Louisville.—p. 452.
Extrapulmonary Tuberculosis. L. Palmer, Louisville.—p. 454.
Treatment of Tuberculosis in Children. O. O. Miller, Louisville.—p. 456.
Discussion of Sprue Syndrome. M. H. Thompson, Louisville.—p. 457.
Surgical Treatment of Peptic Ulcer. J. M. Frehling, Louisville.—p. 460.
Anemia as a Problem for the Dermatologist. H. Gordon, Louisville.—p. 464.

Maine Medical Association Journal, Portland

31:267-290 (Oct.) 1940

- Estimating the Operative Risk. E. E. O'Donnell, Portland.—p. 267.
Pitfalls of Surgery. E. H. Risley, Waterville.—p. 270.
Estimation of Operative Risks and Choice of Anesthesia. G. Clapperton, Lewiston.—p. 274.
Postoperative Management. W. V. Cox, Lewiston.—p. 277.

Michigan State Medical Society Journal, Lansing

39:729-808 (Oct.) 1940

- Jaundice: Differential Diagnosis and Treatment. W. Walters, Rochester, Minn.—p. 747.
Anesthesia in Shock. F. J. Murphy, Detroit.—p. 755.
*Impediment to Circulation: Occasioned by Pulmonic Interstitial Emphysema and Pneumomediastinum. C. C. Macklin, London, Ont.—p. 756.
Carpal Bone Injuries: Conservative Treatment. H. W. Woughter, Flint.—p. 759.
Cancer of Uterus: Plea for Adequate Irradiation. H. S. Collisi, Grand Rapids.—p. 763.
Virus of Poliomyelitis: Survival for Over Six Months in Feces of a Contact. S. D. Kramer, Lansing.—p. 766.
*Hyperactive Carotid Sinus Reflex: Clinical Experiences. B. E. Goodrich, Detroit.—p. 768.
Chronic Sinus Disease: Biologic Factors. R. W. Teed, Ann Arbor.—p. 772.
Lower Leg Fractures: Some Practical Considerations in Treatment. C. E. Maguire, Detroit.—p. 779.
Hydrorrhea Gravidarum. T. Wilensky, Eaton Rapids.—p. 783.
Iodide Content of Iodized Salt: Effect of Storage. D. M. Cowie and J. J. Engelfried, Ann Arbor.—p. 784.
Iodized Table Salt Carton: Analysis of Iodide Content of the Pasteboard. D. M. Cowie and J. J. Engelfried, Ann Arbor.—p. 785.
Meckel's Diverticulum: Invagination. H. A. Hanelin, Marquette.—p. 786.

Impediment to Circulation.—Macklin points out that air may leak into the connective tissue sheaths of the pulmonary arteries and veins from the surrounding alveoli and produce bubbles which interfere with the pulmonary circulation. With continued influx the air may travel along these sheaths to the mediastinum and accumulate there as large blebs which indent the heart and great vessels. The circulatory embarrassment resulting from this aberrant air may be serious and attended by dyspnea and cyanosis, and in children it may cause death. Often it clears up in a fortnight or less. Pulmonic interstitial emphysema is important clinically because of the encroachment by air bubbles on the space of the vascular system. Experimentally the air is propelled along the sheaths by the force of an artificial blast of air, but chiefly it is moved on by respiration, coughing, straining and other acts. Pulmonic interstitial emphysema and pneumomediastinum have been caused by excessive pressure in administering intratracheal anesthesia, which complication may be fatal. Atelectasis is an important primary cause and must always be looked on as a threat of air invasion of the pulmonic vascular sheaths. A tendency to alveolar leakage would seem greater in some individuals than others and may be inherited. Too sudden inflation of a lung at operation may precipitate a leakage. Interstitial emphysemas and their associated pneumothoraces are never spontaneous. There always is an immediate exciting and predisposing cause. Roentgenograms, particularly oblique ones, are of diagnostic aid, and prompt appropriate therapy may save many lives, especially of children.

Hyperactive Carotid Sinus Reflex.—In a group of eighty-four individuals suffering from what appeared to be a hyper-sensitive carotid sinus reflex, Goodrich was able to duplicate the attacks by pressure on the carotid bulb. Sensitivity varied,

so that only in the degree of reaction rather than in kind were some persons abnormal. Sixty-five of the eighty-four persons were men. The entrance complaint ranged from a few transient dizzy sensations to repeated attacks of syncope. Dyspnea, substernal pain, numbness and weakness occurred. Blindness, aphasia or aphonia were reported. Four patients had only gastrointestinal effects, although many had associated gastrointestinal symptoms. Earlier in this study the patients were exhaustively examined and many laboratory and technical tests were performed before a working diagnosis was made and treatment started. This consisted of advising patients to lessen spontaneous stimulation of the carotid sinuses by avoiding tight collars, abrupt motions, looking upward, singing and other activities leading to increased intracarotid pressure or to external mechanical stimulation. Medication to decrease the vagus reactions and to augment the activity of the sympathetic portion of the autonomic nervous system was utilized. Atropine or synthetic related drugs were most commonly used for vagus inhibition. Ephedrine sulfate and in some instances amphetamine sulfate was given and appeared to be helpful. Thyroid was used in the majority of cases. It was continued until all other medication was discontinued. If no symptoms recurred, continued thyroid medication depended on evidences of thyroid need, judged independently of the carotid sinus activity. Demonstrating to the patient that the origin of the attacks was known and that they could be produced at will restored his confidence. Correction of undesirable habits and ways of living resulted in the cessation of symptoms in one instance without any medication. Fifty-three of the eighty-four patients were treated, and thirty-two were completely relieved, thirteen were satisfactorily relieved (the major handicap was avoided), five required continuous treatment and two were not relieved; both of these had severe cerebral damage, and surgical denervation was not advised. Surgical denervation on the right carotid sinus of one patient brought about complete relief for one year, when symptoms recurred and the patient refused further treatment. The author concludes that hypersensitivity of the carotid sinus reflex becomes more frequent with advancing age and in persons with arterial hypertension. The symptoms are frequently considered heart attacks and digitalis, which is often prescribed, further sensitizes the reflex and exaggerates the symptoms. Electrocardiographic records indicate that the vagal effect is involved in the more dramatic symptoms.

New England Journal of Medicine, Boston

223:607-650 (Oct. 17) 1940

- *Prevention of Diabetes. R. E. Haist, J. Campbell and C. H. Best, Toronto.—p. 607.
Thyroglossal Cysts and Sinuses: Study and Report of 198 Cases. R. E. Gross and M. L. Connerley, Boston.—p. 616.
Eczema in Infants and Young Children. L. W. Hill, Boston.—p. 624.
Pathologic Physiology of Bronchial Asthma in Children, with Reference to Role of Infection. H. N. Pratt, Boston.—p. 626.
Treatment of Bronchial Asthma in Children. E. A. Brown, Boston.—p. 629.
Acute Hepatitis, Jaundice and Abnormal Bleeding as Complications of Acute Appendicitis with Perforation. F. A. Simeone and J. D. Stewart, Boston.—p. 632.
Orthopedic Surgery. J. S. Barr, Boston.—p. 634.

Prevention of Diabetes.—Haist and his associates believe that sufficient information is now available to show that the production of diabetes in experimental animals by pituitary diabetogenic substances may be prevented by dietary means or by large doses of insulin. Their studies of the factors which affect the insulin content of the pancreas support those of previous workers who approached the problem from other directions. The experimental prevention of the diabetic condition by certain procedures makes it imperative that their curative effect be investigated. In considering the relation of their results to the treatment of diabetes in human subjects, the authors assume that the factors which prevent the condition from developing will also tend to limit its progress. Fasting, fat-feeding and insulin prevent or hinder the diabetic state under experimental conditions. These procedures affect the pancreas in a manner opposite to that of high carbohydrate diets and prevent the deleterious effects of anterior pituitary diabetogenic principles. There is no evidence that factors which rest the pancreas cause permanent damage to islet cells, whereas factors leading to overactivity may produce permanent changes. If a clinician is

convinced that the patient will be benefited by stimulation of the islet cells, diets rich in carbohydrate are indicated. When such diets are used in animals the islet cells may be protected by providing large amounts of insulin. However, if the physician believes that the pancreas should be rested, fasting, fat-feeding and insulin may be employed. When extensive destruction of the islet cells exists he may decide that there is no point in resorting to these procedures. Under other conditions a reduction of the strain on the remaining islet cells may restore some exhausted cells and thus improve the diabetic condition. This would seem to be particularly true in the early stages of the disease. In animals the exhausted cells retain for some time their ability to recover. The interval during which the cells of man may be exhausted but still be capable of recovery is unknown. Resting procedures prevent the degenerative changes from occurring in cells not already affected and permit restoration of the exhausted cells retaining such ability. Wide departures from the normal diet are permissible for only short intervals. Over longer periods nutritional requirements must be satisfied, especially for growing children, for whom only minor alterations are justifiable, in which case insulin may be the method of choice. The prophylactic administration of insulin to potentially diabetic patients may become an accepted clinical procedure in the future. The authors suggest that the incidence of diabetes should be investigated among two large and comparable groups of children with a familial history of the disease. One group should be given a normal diet and the second a diet as low in carbohydrate and protein and as rich in fat as is physiologically feasible. The second group might be given limited amounts of insulin. The authors appreciate the inherent difficulties of such a clinical investigation but believe that the goal justifies the endeavor.

Public Health Reports, Washington, D. C.

55:1801-1844 (Oct. 4) 1940

Rheumatic Heart Disease in Philadelphia Hospitals: Study of 4,653 Cases of Rheumatic Heart Disease, Rheumatic Fever, Sydenham's Chorea and Subacute Bacterial Endocarditis, Involving 5,921 Admissions to Philadelphia Hospitals from Jan. 1, 1930, to Dec. 31, 1934: IV. Influence of Season and Certain Meteorologic Conditions. O. F. Hedley.—p. 1809.

55:1845-1878 (Oct. 11) 1940

Rheumatic Heart Disease in Philadelphia Hospitals: Study of 4,653 Cases of Rheumatic Heart Disease, Rheumatic Fever, Sydenham's Chorea and Subacute Bacterial Endocarditis, Involving 5,921 Admissions to Philadelphia Hospitals from Jan. 1, 1930, to Dec. 31, 1934: V. Distribution by Locality of Rheumatic Conditions in Philadelphia. O. F. Hedley.—p. 1845.

Rickettsia Diaporica: Its Persistence in Tissues of Ornithodoros Turticata. G. E. Davis.—p. 1862.

Radiology, Syracuse, N. Y.

35:391-520 (Oct.) 1940

Pulmonary Overexpansion in Infancy and Early Childhood. R. A. Carter, Los Angeles.—p. 391.

Quality of Roentgen Rays: Effect on Tissue Dose and Clinical Importance. R. R. Newell, San Francisco.—p. 402.

Calibration of X-Ray Developer. G. M. Busanovich, Philadelphia.—p. 407.

Juvenile Osteochondrosis. C. A. Stammel, Fort Benning, Ga.—p. 413.

Radiation Therapy of Diphtheria Carriers. I. I. Kaplan, New York.—p. 425.

*Preoperative Irradiation in Carcinoma of Breast: Histologic Study. E. P. Halley, Stockton, Calif., and P. J. Melnick, Chicago.—p. 430.

Roentgen Findings in Caisson Disease of Bone: Case Reports. R. A. Rendich and L. A. Harrington, Brooklyn.—p. 439.

Roentgen Ray Examination in Individuals Suffering from Low Back and Sciatic Pain, with Examples of Some Lesions in Which Errors in Diagnosis May Readily Be Made. J. C. Bell, Louisville, Ky.—p. 449.

Myelography with Use of Thorium Dioxide Solution (Thorotrast) as Contrast Medium. B. H. Nichols and W. A. Nosik, Cleveland.—p. 459.

Effect of Iodized Oil on Meninges of Spinal Cord and Brain. L. H. Garland, San Francisco.—p. 467.

X-Ray Therapy of Hyperparathyroidism. E. A. Merritt and R. M. Calk, Washington, D. C.—p. 477.

Sarcoid. E. R. Bader, Cincinnati.—p. 482.

Metastasis to Bone from Carcinoma of Gastrointestinal Tract. J. J. Stein, Hines, Ill.—p. 486.

Graphic Constructions for Localization, Mensuration and Reduction: Standard Symbols and Nomenclature. J. Kaufman, Brooklyn.—p. 489.

Preoperative Irradiation in Carcinoma of Breast.—Halley and Melnick observed radiation necrosis of tumor cells, associated with hyperemia, cellular infiltration, granulation tissue proliferation and fibrous and vascular changes after administration of massive doses in transplantable rat tumors.

After fractional and protracted irradiation the most radiosensitive cells are destroyed by necrosis, but the remaining resistant cells undergo mutation-like alterations. The small daily doses transform them into pleomorphic abnormal forms, giant tumor cells which result from the direct action of radiation on the tumor cells and not from secondary reactive mechanisms. These giant cells do not degenerate by necrosis but by calcium deposition in their nuclei. There is no fibrosis and no vascular damage. Normal tissues recover from the small doses. Much of the fibrosis and vascular obliteration obviously results from damage to normal structures by irradiation at an intensity too high or because of too large individual or total doses to allow normal tissues to recover. In the usual case of carcinoma of the breast amputated from two to three months after irradiation, much intact and uninjured cancer is seen. This has been interpreted by pathologists as tumor tissue which has escaped the action of radiation. The authors think that perhaps the actual irradiation changes which occur earlier were missed. Accordingly, earlier amputation was requested, and data were collected on 21 cases of breast cancer in which tumor doses ranging from 1,200 to 4,500 roentgens were administered over periods of from eleven to forty-nine days. The interval between irradiation and operation ranged from one to forty-five days. Operation was done when desquamation was complete and the skin became smooth and dry, making surgical cleanliness feasible. The microscopic changes in these cases correlate with those found in animal tumors. It seems logical, therefore, to conclude that irradiation by fractional method acts directly on human breast tumor cells by producing early radionecrosis of sensitive cells and later by accumulation of mutation-like effects through succeeding generations of daughter cells. The latter mechanism may easily be the more significant. Damage to the tumor bed does not occur under usual fractional irradiation. Regrowth of surviving tumor cells appears in from four to six weeks after therapy ends. If this is true, it would seem that a short preoperative course of irradiation fails to achieve optimal tumor damage, as the mutation-like effects require from four to five weeks of irradiation. Since tumor bed damage is slight under the fractional method, this mutational mechanism can well be followed to a full second degree cutaneous reaction. Surgery done within two or three weeks after irradiation has the advantage of a tissue in which viable tumor cells have been decreased to a numerical minimum. Further delay faces regrowth of the tumor. After from eight to twelve weeks operation is done with the tumor almost in its preirradiation state, with the probability of invasion and metastasis. There have been no complications in the 21 cases in which operation followed an acute cutaneous erythema. Healing seemed more prompt in the irradiated patients.

Rocky Mountain Medical Journal, Denver

37:717-796 (Oct.) 1940

Mycotic Infection in Northeastern Colorado. A. E. Lubchenko, Sterling, Colo.—p. 741.

Modern Trends in Treatment of Acute Appendicitis. G. S. Postma, Denver.—p. 747.

Management of Labor in the Primipara. C. F. Moon, Omaha.—p. 751.

South Carolina Medical Assn. Journal, Greenville

36:267-300 (Oct.) 1940

Chronic Tetany: Is This Condition Common in Adults? E. B. Poole, Greenville.—p. 267.

Diagnosis and Management of Carcinoma of Colon. R. G. Doughty, Columbia.—p. 272.

Conservative Management of Pelvic Infections. J. A. Sasser, Conway.—p. 276.

Fracture of Skull with Unusual Complications. G. T. Tyler Jr., Greenville.—p. 281.

Tennessee State Medical Assn. Journal, Nashville

33:375-418 (Oct.) 1940

The Acute Abdomen. E. G. Kelly, Memphis.—p. 375.

Medical Participation in Selective Service. C. B. Spruit, Washington, D. C.—p. 382.

Gastrointestinal Symptoms of Urologic Conditions. C. H. Barnwell, Chattanooga.—p. 386.

Some Observations on the State Program for the Relief of Crippled Children. R. W. Billington, Nashville.—p. 393.

Etiology and Treatment of Eczema in Children. W. R. Graves, Memphis.—p. 400.

Private Practice of Public Health. J. C. Overall, Nashville.—p. 405.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Children's Diseases, London

37:153-216 (July-Sept.) 1940

*Observations on Megacolon (Hirschsprung's Disease), with Special Reference to Association with Changes in Fundus Oculi and Hydrocephalus. C. Worster-Drought and J. Shafar.—p. 153.

Tracheotomy Twice for Laryngeal Diphtheria. A. R. Thompson.—p. 166.

Familial Vulnerability of Special Sites Toward Lesions of Congenital Syphilis: Ischemic Disturbance in Fingers of Two Sisters, Probably Due to Third Generation Syphilis. T. Anwyl-Davies, D. Nabarro and F. P. Weber.—p. 173.

Studies on Agglutinins and Agglutinogens in Blood of the Newborn. J. Halbrecht.—p. 175.

Megacolon Associated with Hydrocephalus and Optic Atrophy.—Worster-Drought and Shafar report a case of Hirschsprung's disease associated with hydrocephalus and optic atrophy. The somewhat obese blind boy aged 8 years was born prematurely of apparently normal parents and seemed to be of normal intelligence. He had suffered from obstipation since birth and for the last two years showed abdominal distention, with vomiting and diarrhea during the last year. Fecal discharges occurred every four days and were hard and bulky. A barium sulfate enema disclosed an enormous generalized dilatation of the colon. The encephalogram revealed symmetrical hydrocephalus. The optic fundi presented the picture of advanced bilateral optic atrophy with the vision of the right eye reduced to the mere perception of finger movements and with visual acuity of the left eye at 6/60. The authors, discussing the etiology and pathogenesis of the combined lesions, point out that in Hirschsprung's disease the hypertrophy cannot be accounted for by organic obstruction. The present tendency is to regard megacolon as a neuromuscular dysfunction due to an imbalance between the sympathetic and parasympathetic divisions of the autonomic nervous system. What constitutes the exact nature of the imbalance is still disputed. In hydrocephalus three mechanisms may be involved: (1) obstruction to the circulation of the cerebrospinal fluid, (2) defective absorption and (3) excessive secretion. Obstruction in the pathways of the cerebrospinal fluid is the commonest cause of congenital hydrocephalus and arises either from developmental abnormalities or from inflammatory processes or fibrosis, secondary to intracranial hemorrhage sustained intra partum. Defective absorption may arise from hypothetic infection involving the arachnoid villi or from maldevelopment of these structures. The cause of hypersecretion of cerebrospinal fluid by the choroid plexuses is still *sub judice*. Megacolon and hydrocephalus in the present case are assumed by the authors to have developed in utero. Hydrocephalus was, however, not progressive. Measurements of the circumference and diameter of the skull showed little variation from the normal. The underlying cause was either of a temporary nature or a defect that admitted of compensation. Congenital optic atrophy was regarded by the authors as secondary to hydrocephalus.

British Medical Journal, London

2:479-512 (Oct. 12) 1940

Review of Causes of Diabetes Mellitus. G. Graham.—p. 479.

Changes Occurring in Blood Stored in Different Preservatives. J. Dubash, O. Clegg and Janet Vaughan.—p. 482.

*Methods of Fluid Administration in Treatment of Surgical Shock: Experimental Comparison. R. A. King.—p. 485.

Use of Sulfur-Containing Compounds, Particularly Pentothal Sodium, in Conjunction with Sulfapyridine. E. J. R. Smith.—p. 488.

Use of Proflavine and Acriflavine in a Throat and Nose Department. G. Young and A. A. Charteris.—p. 489.

Fluid Administration for Surgical Shock.—King compared the value of several fluids for the treatment of experimental secondary shock in cats. Temporary recovery readily occurred in most cases of shock on the intravenous addition of physiologic solution of sodium chloride. The rise in blood pressure usually lasted from a few minutes to half an hour, after which it returned to the previous shock level or even lower. In severe shock intravenous physiologic solution of sodium chloride had little or no effect in raising the blood pressure. The rapid passage of the fluid through vascular endo-

thelium into the tissues explains the temporary effect. Therefore the practicality of its use is limited. When too much is given, pulmonary edema occurs. Often about 20 per cent of the normal blood volume can be given in the early stages of shock. Cardiovascular disease and degenerative changes in the vascular endothelium from prolonged anemia and anoxemia greatly increase the risk of pulmonary edema. In order to avoid cardiac failure, intravenous fluids as a rule should be given slowly by the drip method. The risk of pulmonary edema is greatest in the advanced stages of shock. The intravenous administration of hypertonic solutions of sodium chloride in shock causes an immediate rise of blood pressure and the rise is prolonged. The response is sudden and so marked that it bears little relation to the amount of fluid given. The prolonged effect is partly due to the altered osmotic pressure of the plasma in the circulation which causes reabsorption of tissue fluids. Blood pressure in shock can frequently be restored by water absorbed from the intestine. However, in many cases the alimentary canal does not tolerate fluids and vomiting occurs, in which case fluids may be given subcutaneously. Isotonic sodium chloride or dextrose solutions given by subcutaneous injection over a prolonged period restore blood volume and pressure in shock. The effect is prolonged and contrasts remarkably with the temporary benefit obtained from physiologic solution of sodium chloride given intravenously. In certain experiments subcutaneous fluid produced no effect on the blood pressure, and the animals died without showing any signs of recovery. These fatal cases were always severe cases of long standing in which the circulation was probably too stagnant for subcutaneous absorption to occur. Hypotonic solution of sodium chloride by the subcutaneous route was rapidly absorbed in most cases of shock and caused a gradual sustained increase of blood pressure when the circulation was stimulated by hypertonic sodium chloride solutions and when an osmotic gradient was maintained. It is seen from the experiments that the state of shock may be benefited by the addition of fluid to the circulation. The clinical application of the foregoing principles of fluid administration is proceeding. Several cases of severe shock have been treated successfully. In 1 instance the blood pressure recovered from the low level of 30 mm. of mercury.

Lancet, London

2:411-442 (Oct. 5) 1940

*Treatment of Chronic Mastitis. H. J. B. Atkins.—p. 411.

Nomenclature of Influenza. F. L. Horsfall Jr., E. H. Lennette, E. R. Rickard, C. H. Andrewes, W. Smith and C. H. Stuart-Harris.—p. 413.

*Survival of Stored Red Cells After Transfusion. S. R. M. Bushby, A. Kekwick, H. L. Marriott and L. E. H. Whitty.—p. 414.

Survival of Stored Blood After Transfusion. M. Maizels and J. H. Paterson.—p. 417.

Survival of Transfused Erythrocytes of Stored Blood. P. L. Mollison and I. M. Young.—p. 420.

Asthmatic Attack Studied Through the Bronchoscope. A. L. d'Abreu.—p. 421.

Treatment of Chronic Mastitis.—Atkins states that a clinic for the investigation and treatment of chronic mastitis was attended by 212 patients with pain or with lumpiness in the breast. Previously he had defined chronic mastitis as "pain or lumpiness of the breast not due to bacterial inflammation, new growth or fat necrosis," a definition which frankly admits ignorance of the nature of the disorder. Early in the investigation it became clear that slight periodic pain in the breast and lumpiness sufficient to distinguish the breast from the surrounding subcutaneous tissue were commonly encountered among patients who never complained of their breasts. It was concluded therefore that the presence of these two symptoms did not necessarily imply abnormality. The definition of chronic mastitis thus tended to be confused until it was realized from microscopic studies that there was no definite distinction between the normal breast and the breast affected with chronic mastitis, the one merging imperceptibly into the other. A definition which makes such a distinction is undesirable and in fact impossible. In practice the author uses the term "chronic mastitis" to indicate pain or lumpiness in the breast of sufficient degree to bring the patient to the doctor. This implies that there are women experiencing these two symptoms who, because of fear of cancer or from some other psychologic cause, attend the mastitis clinic when their more phlegmatic

sisters with breasts similarly affected stay away. Thus a mastitis clinic becomes to some extent the resort of the apprehensive and the mentally unstable, and in assessing the effect of treatment it is important to take this psychologic element into account. The author did not feel justified in differentiating "mazoplasia" from "chronic cystiphorous epithelial hyperplasia," but the distinction between "epitheliosis" and "adenosis" has been of value in clarifying his idea of the histology of this disease, although he found that these two changes tend to occur together. Because of the psychologic element in painful nodular breast, it is necessary to exercise the most scrupulous control in investigating the effect of the various therapeutic agents. Six of the patients became pregnant while under observation and in 4 of them all symptoms disappeared between the fifth and sixth months. One of these 4 had had mastitis for many years and a previous pregnancy had caused the symptoms to disappear for eighteen months. The author examined the effect of estradiol benzoate given by injection or of the synthetic substance stilbestrol given by mouth. He found that the administration of estrogens in doses sufficiently large to affect the breast was found to be harmful, and it was thought that the microscopic changes were advanced by this substance. Androgens can alleviate the symptoms of most cases of chronic mastitis, but the beneficial effect is not permanent and undesirable concomitant effects, such as hirsuties, changes of voice, amenorrhea or disturbance of menstruation, may rob the treatment of its value. In 1 case of chronic mastitis, the only one of 212 to become malignant, carcinoma of the breast developed ten months after a course of testosterone propionate injections. The microscopic changes in the breast produced by androgens in doses up to the limit of tolerance are insignificant. Diathermy is of value in alleviating the pain in chronic mastitis, but its effect is liable to be only temporary.

Survival of Stored Red Cells After Transfusion.—According to Bushby and his associates, authorities have established organizations for supplying blood in large quantities in preparation for battle and air raid casualties. In the waiting period this stored blood was used for civil practice. Research was concentrated on the finding of diluents, anticoagulants, chemicals and other factors designed to ensure that the red cells would be sufficiently well preserved to survive in the recipient. Whether transfused red cells endure in the recipient cannot be determined by a simple blood count, because it does not show whether rises or falls in a total count are due to autogenous cells or to the transfused blood. The technic employed by the authors was to transfuse group O blood to a group A or group B patient. Counts of the recipient's blood were taken at intervals, a 1:101 dilution being made with the appropriate alpha or beta serum; the titer of the serums so used was 1:320. After being thoroughly mixed in the pipet, the contents were immediately expelled into a corked tube and incubated at 37 C. for an hour, being shaken at intervals of fifteen minutes. At the end of this time a drop was placed on a counting chamber and a count made of the "free" nonagglutinated cells which represent transfused group O cells. Before transfusion, the "nonagglutinable count," that is, the number of A or B cells not agglutinated by the particular alpha or beta serum, was determined for each patient. This number, which is assumed to be constant for each person, is subtracted as a correction from the "free" cell count before the number of surviving group O cells is calculated. The authors show in tables the percentage of cells surviving up to five consecutive days and at times up to twenty-five days, besides the quantitative fragility of the transfused sample and the amount of hemolysis present. When blood is collected into a 3 per cent solution of sodium citrate in the proportion of 100 cc. of citrate to 440 cc. of blood and stored at from 4 to 6 C., the following substances or procedures prolong the period of preservation of the red cells: adjustment of pH to 5 (of no value in practice), dilution and addition of dextrose. Of the single factors, dextrose is the best. The enhancement given by dextrose and dilution, or dextrose plus dilution plus acidification, is recognizable as such, but the degree is not sufficient to justify utilization for practical storage of blood. For the acute hemorrhage and shock of the wounded the prime necessity is to restore blood volume adequately. With restoration

of blood volume the efficiency of such oxygen-carrying elements is automatically increased. Brewer and his collaborators have reported that stored blood (containing dextrose) from ten to fourteen days old is as efficient as fresh blood for the treatment of acute hemorrhage. The survival figures determined by the authors confirm this statement and show that even older blood survives a reasonable time in the recipient and certainly long enough to keep a wounded man alive until he can receive complete surgical treatment. Such was the experience in recent campaigns, during which some 500 transfusions were given of blood from ten to thirty days old.

Anales de la Facultad de Medicina de Montevideo 25:423-770 (Nos. 5-6-7-8) 1940. Partial Index

- Microscopic Prognosis of Nephropathy Due to Mercury. L. A. Surraço.—p. 423.
Obstetric Shock. R. Briquet.—p. 488.
*Obesity with Temporary Hypogenitalism in Prepuberal and Adolescent Age. J. M. Cerviño.—p. 521.
Interchange of Sex Hormones in Parabiosis. E. Fels.—p. 600.
Time as Pathogenic Factor in Experimental Gynecology. A. Lipschütz.—p. 651.
*Anovulatory Cycle in Women. E. Novak.—p. 687.
Allergy in Obstetrics. A. Peralta Ramos.—p. 703.

Obesity with Temporary Hypogenitalism.—Cerviño studied children between the ages of $7\frac{1}{2}$ and 14 years, nine of whom were boys, in whom obesity was associated with hypogenitalism. Some of the cases presented symptoms resembling Fröhlich's syndrome; others were differentiated from the Fröhlich type by a generalized distribution of adipose tissue and an exaggerated development of bones and muscles. Others again belonged to an intermediate type. Hypogenitalism in the cases simulating Fröhlich's syndrome was restored to normal conditions at puberty or later if retardation of puberty occurred. The various features of the clinical picture including personal and familial antecedents, age of onset, evolution, genital pathology, secondary sex characteristics and gynecomastia are discussed. Obesity with hypogenitalism dissimilar to Fröhlich's syndrome was found to date from birth or develop with the growing child and was found to continue after puberty and was observed either to undergo no modifications or to increase or decrease. In these patients the head was large, the cheekbones and chin pronounced and the diameter of the thorax and pelvis large for the age and the body build. The feet gave the impression of a flatfootedness that was only infrequently confirmed roentgenologically. Heredity played a significant part. There was also precocity in dentition and in the ability to walk and talk. The general health was good. The appetite was exaggerated but did not show the predilection for certain foods noted in the cases resembling the Fröhlich type. Laboratory tests indicated normal levels of glycemia or a tendency to hyperglycemia. The author regards obesity with hypogenitalism as due to modifications of the neurohypophyseal system. While the destruction of the anterior lobe by itself has not been demonstrated to induce adiposity, almost always damage to the hypothalamus is concomitantly observed. Damage to the anterior lobe could produce hypogenitalism with low physical stature but not obesity. In the intimate connection between these two organs lies the explanation of many of the symptoms observed in these cases. The transitory cases resembling Fröhlich's syndrome may be due to damage done to the hypothalamus if the regulatory processes of fat, carbohydrate and water metabolism are lodged here. At the same time the function of the hypophysis (anterior lobe) may be normal or excessive. In retarded puberty cases there may exist a temporary hypofunction of the hypophysis. Cases unlike the Fröhlich syndrome in which, besides obesity, is also seen a pronounced development of bone and muscles and occasionally a temporary hypogenitalism suggest hypercorticalism. However, a functional increase of chromophil cells of the anterior pituitary may be involved. Restriction of carbohydrate and fat consumption gives better results in cases dissimilar to the Fröhlich type than in those resembling it.

Anovulation in Women.—Clinical observations of 142 cases of sterility within a three year period enabled Novak to detect thirty-nine cases (age level between 22 and 43 years) in which sterility was due to anovulatory cycles. Anovulatory cycles were noted four times out of ten in patients between 20 and 25 years,

four times out of eleven between 25 and 30, three times out of seven between 30 and 35, four times out of six between 35 and 40 years and four times out of five between 40 and 45 years. Endometrial biopsy, performed in nineteen of the thirty-nine cases within a few days before menstruation, disclosed a non-secretory type of endometrium, with a proliferative activity that varied between clinical pictures corresponding to an early interval phase at one extreme and a marked Swiss cheese type of hyperplasia at the other. In eleven cases some degree of endometrial hyperplasia was encountered. In all cases menstruation was normal or approximately normal, though some showed a tendency to irregular tempo. In others the menstrual amount was above the average, though not pathologic. According to the author, failure of ovulation is to be considered a possible cause of sterility, especially in women approaching middle age. However, it is not usually advisable to perform endometrial biopsy repeatedly in women anxious to conceive lest it frustrate impregnation in a particular cycle. His observations tend to show that some women ovulate with some cycles and not with others, but that more frequently ovulation is likely to be completely in abeyance for considerable periods of time. Functional bleeding of the common type is merely an exaggeration of the anovulatory cycle. Since patients of this group exhibit no other evidences of endocrinopathy and are usually in good general health and since nonovulation may be a sporadic occurrence, therapeutic measures should be conservatively employed. Organotherapy with pregnancy urine preparations has not been successful. The effects of gonadotropic substances in pregnant mare serum on the human ovary have not yet been satisfactorily determined and require further investigation. The key to the riddle of why luteinizing fractions are released in some cycles and not in others seems to be locked up in the anterior pituitary.

Kinderärztliche Praxis, Leipzig

11:243-276 (Aug.) 1940

- *Therapy of Eczema in Nurslings and Small Children. W. Bayer.—p. 243.
Treatment of Asthma with Injection of Serum of Own Blood During Childhood. G. Tamási.—p. 248.
Metrazol Intoxication in Children. T. Varga.—p. 251.
How to Supply Sick Nurslings with Breast Milk. H. Kleinschmidt.—p. 253.
Collaboration of Pediatrician in Diagnosis of Hereditary Defects. T. Brehme.—p. 259.

Therapy of Eczema in Infants.—Bayer reviews various measures employed in the treatment of the eczema of nurslings, giving special attention to the dietetic measures. He thinks that some of the failures in the dietetic treatment are due to the fact that the same diet which has proved effective in some cases is used for all cases and that local measures are neglected. He is in agreement with Rietschel that it is not so much the nature of a diet as the change of the diet that effects improvement. Brushing is a valuable adjunct to the local and dietetic measures. In a disorder in which it is customary to avoid all external irritation, brushing seems at first contradictory, although it has been recommended for the treatment of eczema in adults. The author employed brushing for the first time in the treatment of a child with mild ichthyosis. Salicylic petrolatum and brushing greatly improved the skin of this child. Then the brush treatment was tried on the infiltrated skin of chronic eczema and of neurodermatitis. Unexpected results were obtained. In acute eczema the healthy portions of skin are brushed. The process is continued until the skin becomes red. After the acute stage has been overcome and redness and weeping have disappeared, the eczematous areas are likewise brushed with greater caution in the beginning than are the healthy skin areas. Brushing is particularly effective in cases in which the acute inflammatory stage is rapidly followed by infiltration or in cases in which the skin has become firmly infiltrated and unelastic. From eight to fourteen days of systematic brushings, together with other local treatment, often produces astonishing results in these cases. At the onset of the treatment the brush should be rather soft and, as the treatment progresses, harder brushes are gradually employed. The brushing is done while the child is given its bath and is continued for about ten minutes. During the first few weeks olive oil or liquid petrolatum is added to the water

of the bath. From 1 to 2 teaspoons of the oil is stirred into hot milk and the mixture is added to the bath water. The liquid petrolatum bath is helpful if the skin becomes rough. The brush treatment can be given in the ordinary water bath after the skin has become normal. The redness produced by brushing rapidly disappears and does not cause irritation leading to a flare-up of the inflammation. In addition to widening the capillaries and influencing the lymph stream of the skin, it can be assumed that the brushing also acts on the circulation. The increased blood perfusion of the skin doubtlessly increases the cutaneous metabolism.

Acta Obstet. et Gynec. Scandinavica, Stockholm

20:99-201 (No. 2) 1940

- Ossification of Uterine Tubes. J. Foged.—p. 99.
Myoma and Carcinoma of Corpus Uteri. H. Leissner.—p. 106.
Clinical and Experimental Investigations on Hypophyseal Transplantations. A. Westman.—p. 118.
*Case of Ectopia Cordis in Living Child, Born at Term. P. Kühnel.—p. 128.
Experiences with Scalp Forceps Traction in Treatment of Uterine Atony. P. Kühnel.—p. 139.
Luteinized Granulosa Cell Tumor. C. von Numers.—p. 146.
Curative Process in Ray Treatment of Uterine Cancer According to Stockholm Method. J. J. Chydenius.—p. 157.

Ectopia Cordis in Living Child Born at Term.—Kühnel reports an instance of abdominorachoschisis with total ectopia cordis in a living child born nearly at term. The malformation consisted in a broad slitlike median defect of the upper part of the abdominal wall and the lower part of the thoracic wall through which the heart was protruding. The heart was beating with a normal rhythm and rate outside the chest. The child was delivered spontaneously in cephalic presentation and showed no other malformations. It lived twenty-six hours and died with increasing cyanosis and dyspnea. The necropsy revealed that from the anterior surface of the heart a thin cord extended down to the amniotic membrane of the umbilical cord. Microscopic examination revealed that this cord consisted of amniotic tissue. The abdominal part of the slit was from 5 to 6 cm. in width, but it was not open, being covered by a thin membrane which was made up of an inner peritoneal leaf and an outer amniotic membrane. The thoracic part of the defect ended a little proximally to the middle of the sternum. The anlage of the sternum was defective, only the nucleus of the manubrium and the upper body nucleus being demonstrable. Only the three upper ribs were connected with the sternum. Opinions differ about the cause and development of the congenital ventral defects, but it is generally agreed that the development of these defects begins early in fetal life. The author emphasizes that a distinction has to be made between hernia proper, most often an umbilical hernia with its characteristic hernial sac, and the true cleft malformation, which either is entirely devoid of a sac or in which, as in the reported case, there is merely a thin covering consisting of peritoneum and possibly some amniotic elements. The term "congenital umbilical hernia" the author applies only to the true hernias, in which a greater section of the intestine, perhaps together with other abdominal organs (stomach, liver, and so on), is situated in the hernial sac. In the cleft defects the evenerations usually are far larger and more variegated. Morphologically and genetically these two conditions differ. Umbilical hernia involves the persistence and growth of the hernial anlage that is a physiologic phenomenon in early embryonic life. Up to the ninth to tenth fetal week there is always an intestinal loop present in the umbilical pouch on the abdominal wall. When the abdominal cavity becomes more spacious the entire length of the intestine is again withdrawn into the abdominal cavity. When this retraction of the intestine into the abdominal cavity is not complete, the result is "physiologic" umbilical hernia. Incomplete closing of the anterior body wall is a true malformation. Little is known about the etiology of these congenital defects, but it can be established that the incomplete fusion of the fetal abdominal wall originates early (about the fourth week) and that these defects are rare. It has been estimated that, whereas a large congenital umbilical hernia is seen about once in 5,000 fetuses, a cleft abdomen is seen only once in 17,000 and the combined abdominorachic defect is even more rare.

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SHOULD SERUM BE USED IN ADDITION TO SULFAPYRIDINE

IN THE TREATMENT OF PNEUMOCOCCIC PNEUMONIA?

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The value of specific serum in the treatment of pneumococcic pneumonia has been recognized for many years. Recently the effectiveness of sulfapyridine in this disease has become equally well established. The indications for the employment of each of these therapeutic agents, the methods of administration, the results to be expected from their use and the possible toxic effects are by now almost universally known. What is not known, however, is the relative value of the two agents when either is used alone or when they are administered in combination.

In table 1 are shown the results of treatment with serum alone as compared with those following treatment with sulfapyridine alone in several clinics where comparative studies have been made. Pneumococci of all types were represented among the causative agents in these cases. Volini, Levitt and Campione¹ reported that 15, or 9.8 per cent, of 153 patients treated with specific serum died, as compared with two (3.3 per cent) deaths among 60 sulfapyridine-treated patients. Although complete data are not given, the disease seems to have been of equal severity in the two groups.

We² found a 16.7 per cent mortality rate, sixteen deaths among 96 patients treated with serum alone, as compared with a mortality rate of 11 per cent, fifteen deaths among 136 patients treated with sulfapyridine alone. The pneumonias were considered to be of approximately equal severity in the two groups, although there were possibly a few more mild pneumonias in the sulfapyridine-treated than in the serum-treated group.

Finland, Spring and Lowell³ treated 211 patients with specific serum, of whom 28, or 13.3 per cent, died. Among 225 patients treated with sulfapyridine alone, 40 died, giving a mortality rate of 17.8 per cent. The authors state that at first sulfapyridine was given only in the milder cases but that later its use was extended to all cases.

Rueggsegger, Hamburger and Cockrell⁴ reported a series of cases which had been treated alternately with serum and with sulfapyridine, respectively. Two (4.4 per cent) of 45 patients treated with serum died and 6 (12 per cent) among 49 patients receiving sulfapyridine. The age distribution of the patients and the percentage of patients with bacteremia was approximately the same for the two groups.

Bullowa and his co-workers⁵ rotated patients after type identification, treating some with serum alone, others with sulfapyridine alone, and others with the combination of the two. There were nineteen deaths among 111 patients treated with serum alone—a mortality rate of 17.3 per cent. Among the 124 patients treated with sulfapyridine alone, 10, or 8.1 per cent, died.

Among a total of 616 patients treated by all these investigators with serum alone 80, or 13 per cent, died; while among the 594 patients treated with sulfapyridine alone 73, or 12.3 per cent, died. As measured by mortality rates, therefore, the results of patients treated with sulfapyridine alone are approximately the same as those following treatment with specific serum alone.

Since sulfapyridine has been found to influence recovery from pneumonia by causing bacteriostasis of the pneumococci⁶ and since it apparently does not increase antibody formation in the host,⁷ one may assume that specific serum, by introducing passive antibodies into the host, would be a valuable adjunct to

3. Finland, M.; Spring, W. C., Jr., and Lowell, F. C.: Specific Treatment of the Pneumococcal Pneumonias: An Analysis of the Results of Serum Therapy and Chemotherapy at the Boston City Hospital from July 1938 Through June 1939, *Ann. Int. Med.* **13**: 1567-1593 (March) 1940.

4. Rueggsegger, J. M.; Hamburger, M., and Cockrell, S. L.: The Comparative Use of Sulfapyridine and Specific Serum in Pneumococcal Pneumonia, *Ohio State M. J.* **36**: 257-261 (March) 1940.

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drug therapy. In order to test this hypothesis, Spring, Lowell and Finland⁸ performed in vitro experiments by means of the pneumococcal test. They found that killing of pneumococci occurred more readily when specific serum and sulfapyridine were used in combination than when either one was used alone. Bullowa and his associates⁵ reached the same conclusion by the use of bone marrow cultures of pneumococci.

Several investigators have studied this problem in animals. Maclean, Rogers and Fleming⁹ found that 25 mg. of sulfapyridine was insufficient to protect mice

TABLE 1.—Pneumonia Patients Treated with Serum Alone Compared with Those Treated with Sulfapyridine Alone

Reported by	Specific Serum			Sulfapyridine		
	No. of Cases	No. Died	Per Cent Died	No. of Cases	No. Died	Per Cent Died
Vollni et al. ¹	153	15	9.8	60	2	3.3
Dowling and Abernethy ²	96	16	16.7	136	15	11.0
Finland et al. ³	211	28	13.3	225	40	17.8
Ruegger et al. ⁴	45	2	4.4	49	6	12.0
Bullowa et al. ⁵	111	19	17.3	124	10	8.1
Total.....	616	80	13.0	594	73	12.3

injected with 100 minimum lethal doses of type VIII pneumococci. When mice were vaccinated with killed pneumococci of the same type and seven days later given 100 minimum lethal doses they likewise died. However, if mice were vaccinated and seven days later received the infecting dose and also sulfapyridine, all of them survived. They were apparently fortified with antibodies from the vaccination and in addition had the advantage of the bacteriostasis caused by the drug.

Kepl and Gunn¹⁰ produced pneumonia in rats with type I pneumococci and treated some with sulfapyridine alone, some with serum alone and others with a combination of the two. Measured by mortality rates and by the length of survival among the animals that died, the best results were obtained in the group which received both serum and sulfapyridine. However, when Wright and Gunn¹¹ used the same methods to produce pneumonia with type III pneumococci there was no significant difference in the mortality rate following the use of serum and sulfapyridine combined, as compared with the mortality rate following the use of sulfapyridine alone.

Powell and Jamieson¹² infected groups of rats intraperitoneally with type I, II, V, VII, VIII and XIV pneumococci. In all types, with the possible exception of type VIII, the combination of sulfapyridine and specific serum resulted in a higher percentage of survivals than either agent used alone.

MacLeod¹³ found that sulfapyridine and serum were synergistic in infections caused by type III pneumococci in mice, since the number of survivors was greater when the combination was used for treatment than when either agent was used alone.

In view of the favorable results obtained by using serum in addition to sulfapyridine in vitro and in animal infections, the present study was undertaken to determine whether the same synergistic action would be obtained in a series of patients with pneumonia caused by pneumococci of types I through VIII.

MATERIALS AND METHODS

The patients were alternated between sulfapyridine therapy and specific serum plus sulfapyridine, as follows: As soon as a patient was admitted to the wards of Gallinger Municipal Hospital and the diagnosis of pneumonia suspected, the sputum was typed and a blood culture taken. No treatment, other than symptomatic, was given until a pneumococcus or other etiologic organism was obtained. If a pneumococcus belonging to one of the first eight types was identified, alternate treatment was given within each type, one patient being given sulfapyridine alone and the next sulfapyridine plus specific antipneumococcus serum.¹⁴ No exceptions to the strict alternation of cases were made on the basis of severity of the disease. Occasionally, when a patient was demonstrated by means of intradermal and intravenous tests to be hypersensitive to both horse and rabbit serum, that patient was given sulfapyridine alone and the next two patients in sequence were given the combination of sulfapyridine and serum, so that the series might be even again. This procedure was also employed for the few occasions when a patient had been started on one or the other therapeutic regimen and was subsequently found not to have pneumonia. A patient receiving any serum which was subsequently discontinued because of hypersensitiveness was nevertheless classified as having received combined therapy. If no type of pneumococcus was obtained from the sputum within six hours, treatment with sulfapyridine was begun and the case entirely omitted from the series.

TABLE 2.—Mortality Rates of Pneumonia Patients Treated with Sulfapyridine Alone and in Combination with Specific Serum

Type	Sulfapyridine			Serum Plus Sulfapyridine		
	No. of Cases	No. Died	Per Cent Died	No. of Cases	No. Died	Per Cent Died
I.....	23	3	22	2
II.....	9	0	10	0
III.....	15	4	16	5
IV.....	6	1	6	0
V.....	3	0	3	0
VI.....	2	1	2	0
VII.....	13	1	13	1
VIII.....	9	0	10	0
All cases.....	80	10	12.5	82	8	9.8
All except type III.....	65	6	9.2	66	3	4.5

There was no fixed dosage schedule for serum. The initial dosage was usually 100,000 units, but often a larger or smaller initial dose was given, depending on the severity of the illness and the duration at the time treatment was begun. If the patient did not show considerable improvement within twelve to twenty-four hours, or if pneumococci were cultured from the blood stream, additional serum was given. The average total dosage of serum per patient was 141,000 units. Thus it is evident that these patients received about the same doses of serum that they would have been given if serum had been administered without sulfapyridine.

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14. Supplied by the Lederle Laboratories, Inc., through the courtesy of Dr. W. G. Malcolm.

The initial dose of sulfapyridine was 4 Gm. by mouth, followed by 1 Gm. every four hours until the temperature reached normal and remained so for three or four days. From that point on, the dose was gradually decreased and the drug finally discontinued after about six days of normal temperature. In the more severely ill patients the first treatment consisted of an intravenous injection of from 3.5 to 4 Gm. of sodium sulfapyridine.

TABLE 3.—Effect of Certain Factors on Mortality Rate

	Sulfapyridine			Serum Plus Sulfapyridine		
	No. of Cases	Died	Per Cent Died	No. of Cases	Died	Per Cent Died
Age of the patient						
12 to 39.....	49	0	0	54	3	5.5
40 and over.....	31	10	32.3	28	5	17.8
Percentage over 40.....	38.6	34.1
Area of lung involvement						
One lobe.....	69	8	11.3	64	2	3.1
More than 1 lobe.....	20	2	10.0	18	6	33.3
Percentage over 1 lobe....	23.0	21.9
Blood culture						
No bacteremia.....	62	7	11.3	66	6	9.1
Bacteremia.....	18	3	16.7	16	2	12.5
Percentage bacteremic....	22.5	19.5
Day treatment begun						
First 4 days.....	47	3	6.4	38	1	2.6
Fifth day or later.....	33	7	21.2	44	7	15.9
Percentage after 4th day	41.3	53.6
Complicating diseases						
Uncomplicated.....	66	4	6.1	65	1	1.5
Complicated.....	14	6	42.8	17	7	43.7
Percentage complicated..	17.5	20.7

Whenever the oral administration of sulfapyridine resulted in low blood levels, it was supplemented by the sodium salt intravenously unless the temperature had already fallen and remained down. The average total dose of sulfapyridine per patient was 40 Gm. among the patients receiving the drug alone and 36.9 Gm. among the patients receiving serum in addition.

RESULTS

In table 2 are shown the mortality rates by type. There were ten deaths among the 80 patients treated with sulfapyridine alone—a mortality rate of 12.5 per cent. Among the 82 patients treated with the combination of serum and sulfapyridine there were eight deaths, or 9.8 per cent. In each group of cases caused by an individual type of pneumococcus (with the exception of the cases caused by type III pneumococci) the mortality rate was the same or lower for patients treated with the combined method than for those treated with sulfapyridine alone. If the type III cases are excluded, there were six, or 9.2 per cent, deaths among the 65 patients treated with sulfapyridine and only three, or 4.5 per cent, among the 66 patients treated with sulfapyridine plus serum.

Thus it appears that when a comparison is made of the sulfapyridine-treated group as a whole with the combined therapy group as a whole, only a slight difference in mortality rate is evident in favor of the combined therapy group. However, when an analysis is made of the cases on the basis of several factors of importance in pneumonia, differences between the two groups become more apparent. These factors, which are shown in table 3, are age of the patient, area of lungs involved, the presence of bacteremia, the day of the disease on which treatment was begun and the presence of complicating diseases.

These data show, first of all, that the cases in the two groups were of about the same degree of severity. While a slightly higher percentage of patients treated

with the drug alone (as compared with those given the combination therapy) were over 40 years of age, had more than one lobe involved and had organisms in the blood stream, on the other hand a slightly higher proportion of patients receiving the combination treatment were treated after the fourth day of the disease and had other diseases complicating the pneumonia. These complicating conditions included acute alcoholism, congestive heart failure, diabetes mellitus, uremia, asthma, tuberculosis and pregnancy.

Among the patients under 40 years of age there were no deaths in the group of 49 who received sulfapyridine alone and only three (or 5.5 per cent) in the group of 54 patients who received serum plus sulfapyridine. There was a more striking difference among the patients over 40 years of age. Of the 31 patients in this group who received sulfapyridine alone 10, or 32.3 per cent, died, while among the 26 patients receiving serum plus sulfapyridine there were five, or 17.8 per cent, deaths. Thus the mortality rate of patients over 40 years of age was nearly twice as great for patients receiving sulfapyridine alone as for patients receiving sulfapyridine in combination with serum.

There were eight deaths (13.3 per cent) among the 60 patients in the sulfapyridine-treated series with one lobe involved and two, or 3.1 per cent, deaths among the 64 patients with one lobe involved who were given combined therapy. When more than one lobe was involved, the mortality rate was greater for those treated by the combined method (33⅓ per cent) compared with 10 per cent for those given the drug alone.

There was little difference in the two groups in relation to the presence or absence of bacteremia. There was an 11.3 per cent mortality rate among the sulfapyridine-treated patients with negative blood cultures and a 9.1 per cent mortality rate among those treated with serum plus sulfapyridine. In the group with bacteremia, 16.7 per cent of those receiving the drug alone died and 12.5 per cent of those receiving the drug plus serum.

Only 1 patient died (2.6 per cent of 38 cases) whose treatment with the combination of drug and serum was begun in the first four days of the disease, while 3 patients, or 6.4 per cent, died among the 47 given the

TABLE 4.—Rapidity of Crisis

Method of Treatment	No. of Patients Recovering	Crisis in 12 Hours		Crisis in 24 Hours	
		Number	Per Cent	Number	Per Cent
Sulfapyridine.....	70	12	17.1	28	40.0
Serum plus sulfapyridine....	74	28	37.8	44	59.5

drug alone at this stage of the disease. Among the cases in which treatment was begun after the fourth day of the disease, 21.2 per cent died when treated with sulfapyridine alone and 15.9 per cent died among those treated with sulfapyridine plus serum.

Among the patients whose pneumonia was uncomplicated by any other disease, 4 (or 6.1 per cent) died after receiving the drug alone, and only 1 (or 1.5 per cent) died among those receiving the drug plus serum. The mortality rates for the patients who suffered from other diseases along with pneumonia were practically the same for the two groups: 42.8 per cent for those receiving the drug and 43.7 per cent for those receiving combination therapy.

In table 4 is shown the relative speed with which the temperature reached a permanent level below 100 F. in the two groups. Within twelve hours after treatment was begun the temperature was below 100 in 12, or 17.1 per cent, of the 70 patients who recovered after treatment with sulfapyridine alone, as compared with 28, or 37.8 per cent, of the 74 patients who recovered after the combined treatment. After twenty-four hours the percentage of patients whose temperature was below 100 F. was still greater (59.5 per cent) in the group receiving sulfapyridine plus serum than it was (40.0 per cent) in the group that received sulfapyridine alone. These rapid crises occurred more frequently in the patients who received the combined treatment in spite of the fact that many of the sulfapyridine-treated patients received their initial dose of sulfapyridine by vein, whereas the initial intravenous dose was seldom given to the patients who received serum also.

COMMENT

On the basis of the results obtained *in vitro* and in animal experiments, one would expect to find, among patients treated with serum plus sulfapyridine a definite lowering of the mortality rate below that obtained when sulfapyridine was used alone. The two studies reported in which cases of pneumonia have been rotated for treatment by these two regimens do not seem to bear this out. Don and his associates¹⁵ reported on patients with type I and II pneumococcus pneumonia alternated in this manner. Among 49 patients who received sulfapyridine alone only 1 died, whereas there were three deaths among 37 patients treated with sulfapyridine plus specific serum. However, the dose of serum used was small, since patients under 40 years of age admitted within ninety-six hours of the onset received only 50,000 units and all other patients 100,000 units. No additional doses were given regardless of the course of the disease. This dosage would not be considered adequate for many patients receiving serum alone as treatment for pneumonia. Furthermore, the authors state that patients admitted during the night were started on sulfapyridine immediately and typing was postponed until the following morning. One wonders whether the treatment in the combined serum-sulfapyridine cases would not have been more effective if treatment with the two agents had been commenced at the same time.

Bullowa and his associates⁶ gave sulfapyridine to 124 patients, of whom 10, or 8.1 per cent, died, while 89 patients were treated with serum plus sulfapyridine with ten, or 11.2 per cent, deaths. When patients treated in the first four days of the disease were considered, there were five deaths among 53 patients given sulfapyridine alone and only one death among the 39 patients treated with sulfapyridine plus specific serum.

Our results show a slightly lower mortality rate when serum was used in addition to the drug than when sulfapyridine was used alone. When the type III cases are omitted, the results are still more favorable for the combined therapy group. The omission of type III cases may well be justified on the ground that there is no report, as far as we are aware, of any significant group of type III cases in which the mortality rate has

been definitely lowered by serum therapy. On the other hand, the prognosis in this type of pneumonia is particularly poor, the mortality rate being as high as, or higher than, that for pneumonia caused by any other type of pneumococcus. Even when sulfapyridine is administered, the death rate is still high. In our own experience there have been fourteen deaths, or 22.6 per cent, among a total of 62 type III pneumonias treated with sulfapyridine, alone or in combination with serum. These facts should stimulate further attempts to lower the mortality rate in this type of pneumonia by combined serum and sulfapyridine therapy.

Although bacteremia is one of the factors which profoundly affect the prognosis in pneumonia, the results obtained in the present series seem to show that sulfapyridine is equally effective when used alone or combined with serum. It has been repeatedly recommended that serum be given in addition to sulfapyridine when bacteremia is present. Our observations tend to question the necessity for this, unless other factors which make for a poor prognosis are present.

Serum seems to be particularly effective as an adjunct to sulfapyridine in patients over 40 years of age and in patients with only one lobe involved, especially when these patients are treated early in the disease. Since the death rate from pneumonia has been repeatedly found to increase progressively with the age of the patient, the superior advantage of combined therapy in the older age group is most welcome.

The relative cheapness and ease of administration of sulfapyridine will make it the method of choice in all cases except those in which it is definitely contraindicated. If our results are confirmed by other similar studies, they would suggest that every patient over 40 years of age seen within the first four days of the disease receive serum in addition to sulfapyridine. After the fourth day of the disease the value of serum as an adjunct is less. In order to give the patient the benefit of every possible aid, however, massive doses of serum might be given along with sulfapyridine to severely ill patients seen late in the disease. Sputum should be obtained for typing and blood taken for culture in every case before sulfapyridine is started, so that serum may be given, whenever it is indicated, as soon as the type is determined. This is necessary in order that the utmost advantage may be taken of the superior results achieved by the earliest possible administration of serum.

SUMMARY AND CONCLUSIONS

1. A series of cases of pneumonia caused by pneumococcus type I through type VIII have been alternated for treatment with sulfapyridine alone and with sulfapyridine plus specific antipneumococcus serum. The mortality rate was 12.5 per cent in the group receiving sulfapyridine alone and 9.8 per cent in the group receiving serum plus sulfapyridine. If the type III cases are omitted, the corresponding figures are 9.2 and 4.5 per cent, respectively.

2. Serum seemed to be particularly valuable as an adjunct to sulfapyridine in patients over 40 years of age.

3. Crisis occurred more frequently and was more prompt in the patients receiving serum in addition to sulfapyridine.

4. It is suggested that serum and sulfapyridine both be given to patients over 40 years of age with pneumonia and to those who are in need of a prompt defervescence.

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EARLY OPERATION (SPINE FUSION) IN
UNSTABLE LUMBOSACRAL JOINTS

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The problem of treating patients with the primary complaint of low back pain, often with sciatic radiation, continues to harass the orthopedic surgeon. This is true not only because of the difficulties in diagnosis so aptly expressed by Steindler¹ when he states that "It [backache] shares with the symptoms of headache the distinction of having almost unlimited possibilities of interpretation" but also because "So long as surgeons disagree in regard to the pathogenesis of chronic low back pain, there cannot be any uniformity of opinion concerning treatment" (Compere²). In spite of these limitations, the orthopedist is repeatedly called on to determine the etiology of this syndrome and then must he decide on whether to follow conservative or radical therapy.

Among younger patients with low back pain due to an unstable lumbosacral joint we at the clinic have been impressed with the results obtained from lumbosacral fusion and dismayed by the difficulty of achieving relief of symptoms through conservative methods on older poor risk patients who likewise exhibit an unstable lumbosacral articulation as well as marked degenerative changes in this area of the spine. It therefore occurred to me that some worth while information might be gained through a study of two groups of patients with low back pain due in my opinion to similar etiology—an unstable lumbosacral joint: group 1, older persons who had received conservative treatment over a period of years of which one year, if not the entire interval, was under personal supervision; group 2, younger patients treated by arthrodesing operations. Obviously, the two groups of patients are not directly comparable, but there is a definite similarity in respect to the history of onset and subsequent backache symptoms during the same age cycle, together with the degree of disability in this period which offers a reasonable basis for study. To clarify the situation, no patient is included with a clinical history or physical examination (including lumbar puncture, and, when indicated, spinogram study) that indicated herniation of an intervertebral disk.

GENERAL CONSIDERATIONS

Space does not permit a detailed discussion of the anatomic, physiologic and pathologic (as far as is known) factors of low back pain. These aspects have been extensively discussed in the literature. However, certain general considerations may be stated that indicate the basis for the approach to the problem.

I agree with Willis³ that "to understand properly the anatomical structures of the lower back and to appreciate its susceptibility to aches of obscure etiology, consideration must begin with the manner in which the lower extremities become attached to the vertebral column. In the evolution of man the pelvis has progressed toward the head by incorporation of the sacrum

and successive last number of vertebrae, the next preceding segment thereupon assuming the characteristics of the last lumbar segment." Of particular interest are the variations in the formation and articulation of the last lumbar and first sacral segments, where anomalies are common to all vertebrates and are, in the main, steps in an evolutionary shortening or lengthening of the presacral column. Variation in the number of presacral segments is of little importance in a discussion of backache, whereas the presence of asymmetrical sacralization and defective lumbosacral articulations is of definite interest in that they provide points of lessened resistance to stress and strain and, with a definite susceptibility, to muscle and ligament injury. Furthermore, the lumbosacral region is inherently weak "because as a structure developed for quadrupedal function with a support under either end of it [the spine] has been forced to manage a right angle turn and balance in the upright position, thereby acquiring mechanical imperfection and areas of exaggerated stress."

I therefore support the clinical concept advanced by Ferguson⁴ in 1925 and published in 1934 that lumbo-



Fig. 1.—The arrows indicate the most stable type of lumbosacral articular facets, namely when the articular surfaces face internal-external in relation to the midline of the body.

sacral anomalies produce symptoms only through faulty mechanics. As long as the muscles and ligaments are of sufficient strength and tone to enable the person to continue in his environment without fatigue there are no symptoms; that is, the patient is "compensated." Decomensation, and hence back pain, results from failure of the muscles and ligaments to support the lumbosacral area. This is particularly prone to occur in a spine which exhibits faulty mechanical structure because these muscles and ligaments "have less than normal capacity for meeting extraneous stress and strain since a certain portion of their total capacity is already in use." This conception is especially well borne out in the type of case here reported (group 1), which illustrates the fact that as one grows older the muscles lose their tone and power. In consequence, the person well compensated at 20 may at 40 not have sufficient muscle power to protect the lower part of the back from strains that were easily met in earlier years.

Since the principal cause of low back pain in these cases is fatigue strain in the soft tissues resulting from

From the Department of Bone and Joint Surgery, the Lahey Clinic. Read before the Section on Orthopedic Surgery at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

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the structurally faulty mechanical construction or abnormally close relations of the bony parts, such a condition will often affect one side more than the other, or even one side alone. Furthermore, symptoms from the stress and strain need not be on the same side as the bony anomaly, for the most potent irritating factor is not

acquired and is due either to trauma, such as a heavy fall on the buttocks, or to degenerative changes in the disk, the result of faulty posture. Williams⁷ believes that this condition explains posterior displacement of the fifth lumbar on the first sacral vertebra, because settling of the disk segment takes place in a down and backward plane guided by the inclination of the sacral facets, and the more acute the lumbosacral angle the more marked is the posterior tilt of the first sacral facet and thus the greater the posterior displacement of the fifth lumbar vertebra.

POSTERIOR DISPLACEMENT OF THE FIFTH LUM- BAR VERTEBRA

It is my opinion that posterior displacement of the fifth lumbar vertebra on the sacrum is an entity and not an illusion. Repeated study of roentgenograms indicates that the decision

on this point lies in obtaining true lateral views of the lumbosacral area. When one is in doubt as to the presence of this anomaly, as these displacements are variable, a comparison of true lateral roentgenograms in extreme flexion and again in hyperextension of the lumbosacral spine and hip joint will decide the question.

Ferguson states that the mechanism of posterior displacement of the fifth lumbar vertebra on the sacrum occurs as follows: In the presence of a hypermobile lumbosacral joint due to the coronal type of articular facets, on hyperextension the fifth lumbar glides backward on the first sacral vertebra—an exaggeration of the normal motion—while on flexion, instead



Fig. 2.—a, Unstable asymmetrical lumbosacral articular facets with rudimentary articular processes. b, Another example of very unstable asymmetrical facets, the joint surfaces facing superior-inferior. Note productive bone change about these articulations.

necessarily the most obvious anomaly in the roentgenogram. Badgley⁵ and Hodges and Peck⁶ also emphasized this point in a study of 447 patients, of whom 27 per cent who complained of low back pain had anomalies of the lumbosacral region as opposed to 14.3 per cent with anomalies in a symptom-free control group.

DEFINITION

The term unstable lumbosacral joint is descriptive of a clinical entity which includes any arrangement of bony parts at the lumbosacral junction that is not adequate for support without undue stress or strain on the adjacent muscles and ligaments (Ferguson). Such an arrangement comprises one or more of the following mechanical faults: unstable lumbosacral facets (including rudimentary articular processes), bone defects in the posterior elements of the lumbosacral vertebrae, transitional vertebrae (sacralization and lumbarization), spondylolisthesis, abnormally acute lumbosacral angle and posterior displacement of the fifth lumbar vertebra on the sacrum.

A narrow lumbosacral disk may also be observed. Two types are recognized. One is congenital and is found in normal sacralization wherein the vertical diameter of the disk may vary between the diameter of the usual thick lumbosacral type and that of the thin sacral disk, as pointed out by Willis. It is doubtful whether this type is a cause of pain. The second type is

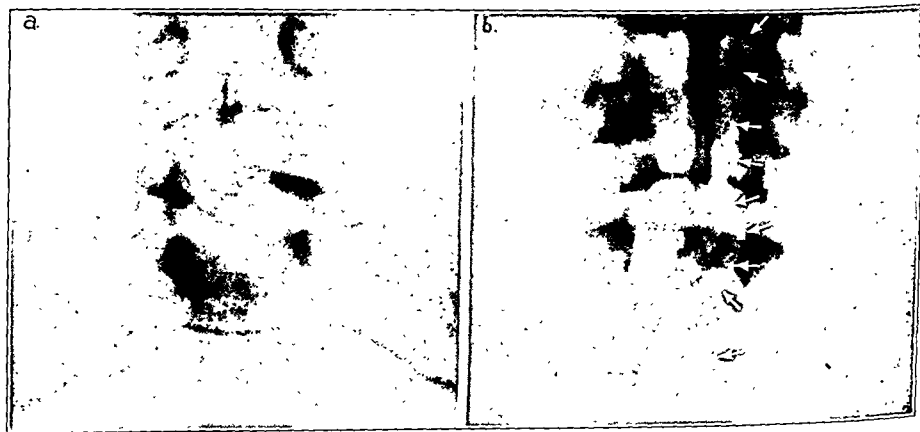


Fig. 3.—Bone defect in posterior elements of the lumbosacral vertebra. a, Usual anteroposterior view. b, View at 45 degree angle, same patient, illustrating the effective value of this film to show the defect.

of gliding forward, the fifth lumbar tilts forward as it is caught in the position of posterior displacement. Finally I believe that, as a minimum, 95 per cent of patients with chronic low back pain are best treated by a conservative regimen. This statement does not include pathologic conditions of the spine such as tuberculosis, primary neoplasms, fractures, osteitis or her-

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niated disks. Thus among 2,000 patients with pain low in the back who were seen at the clinic from January 1936 to January 1939 fifty, or 2.5 per cent, were submitted to arthrodesing operations.

But it is also my opinion that in emotionally balanced younger patients of the age group from 30 to 45 years

85 per cent were between 31 and 35 years old. The fourth decade is the period when previously well functioning (that is, compensated) muscles and ligaments begin to weaken from lack of use. Then decompensation of these soft parts takes place and back symptoms result. It is also important to bear in mind not only

that these patients have experienced years of low back pain with attendant repeated efforts to ameliorate symptoms but also that in this interval all have accepted a definite reduction in the degree of their usual physical activities. This limitation is well expressed in the summary of the words of one patient: "I realized I had a weak back and therefore avoided activities that I thought might cause an acute attack or intensify my chronic low back pain."

The treatment of these patients in this clinic as well as elsewhere included all the methods of conservative

therapy with which we are familiar. Of effective methods there was one common denominator, namely bed rest. In many instances it is quite probable that persons would have experienced comparatively slight disability if they had carried out instructions consistently, especially in regard to muscle exercise and diet to reduce weight. But in our experience it is an exceptional patient who for years will follow such a regimen. Therefore, a younger person with low back pain due to an unstable lumbosacral joint not relieved by a trial

with persistent low back pain due to an unstable lumbosacral joint, and in whom a trial of adequate conservative therapy has not been successful, fusion of this articulation should be offered as a preferred method of treatment. Arthrodesis is indicated rather than to have the patient accept an often marked degree of permanent limitation of activities while he continues to experiment with various supports and different forms of physical therapy, as well as visiting a series of physicians in his effort to be rid of periodic bouts of severe low back pain.

ANALYSIS OF CASES

GROUP 1.—Herewith is a summary of the observations on seventy-five patients (fifty-four women, twenty-one men), average age 52, who had experienced disabling low back pain owing to an unstable lumbosacral joint over a period of from ten to fifteen years. In every case there was roentgenographic evidence of productive bone changes at the unstable articulation. Generalized degenerative arthritis of the lumbar spine was noted in eighteen cases of this group. This consistent finding of degenerative bone changes about unstable lumbosacral joints is significant not only as indicative of the mechanical unsoundness of the joint but also because this arthritis, when established, is an additional factor in the production of symptoms. Such arthritic pain would in turn have been avoided by a fusion operation earlier in life.

The onset of persistent low back symptoms in this group occurred in the age interval of 30 to 40 years;

of conservative therapy, should, I believe, be asked seriously to consider and, if possible, have a fusion operation performed, because a lumbosacral arthrodesis, when successfully carried out, eliminates the etiologic mechanical factor as well as preventing development of degenerative arthritic changes at the lumbosacral joint.

GROUP 2.—The following data summarize the results of arthrodesing operations on fifty patients (thirty-four



Fig. 4.—a, Transitional vertebra illustrating unilateral incomplete sacralization. Note rudimentary type of articular processes and also the bone condensation about pseudarthrosis. b, Three years after lumbosacral spine fusion. Complete relief of low back symptoms of four years' duration in a woman aged 32. Note also that the sacralized process has fused to the sacrum.

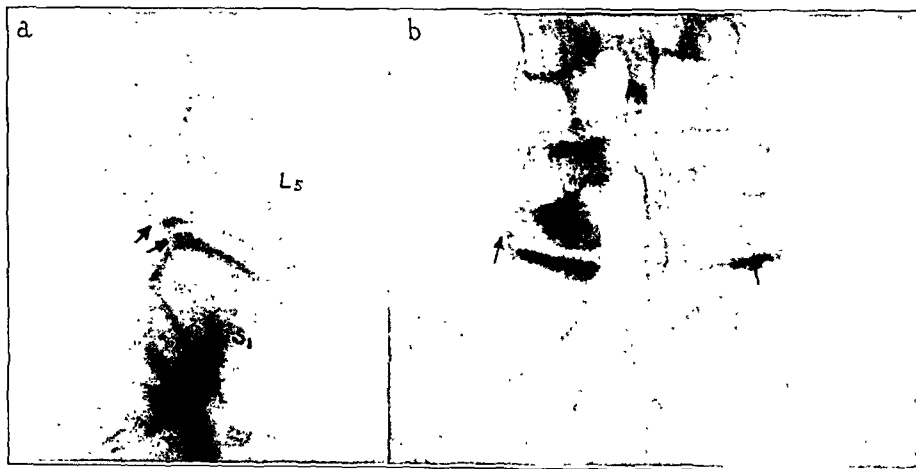


Fig. 5.—a, Illustrating definite posterior displacement of the fifth lumbar vertebra on the sacrum, with narrow intervertebral disk. Marked disability in a man aged 45. b, Anteroposterior view of the same patient. Note productive bone changes about the unstable lumbosacral articular facets which are of the anteroposterior type.

women, sixteen men), with an average age of 36 years, all with severe low back pain due to an unstable lumbosacral articulation. The average age at onset of symptoms was 32 years. Each of these patients had received an adequate trial of conservative therapy without permanent relief. Forty-six patients, or 92 per cent, were relieved of their back symptoms after spine fusion (from eighteen months to three years follow-up). There were four failures due to poor selection of cases. Two patients exhibited chronic arthritis originally thought to be localized at the lumbosacral joint but which proved to be a progressive process and spread to other levels of the spine. One patient was definitely a psychiatric subject, and this condition was not recognized in time to prevent the operation, and one patient who has a compensation problem has obtained no relief and, in my opinion, will not until definite arrangements are made for a pension. A postoperative roentgenogram on this patient shows a firm fusion.

CONCLUSIONS

1. The majority of patients with chronic low back pain can be relieved of their symptoms by conservative measures.

2. As a result of experience with one type of case—in which symptoms are due to an unstable lumbosacral joint—I believe that if a definitive trial of conservative treatment does not relieve symptoms, or if the mechanical arrangement of the bony part is very faulty, as for example in pronounced spondylolisthesis, then an arthrodesis of the lumbosacral spine is the best method of treatment.

Spine fusion is indicated because in these cases the pain and disability result from failure of the adjacent muscles and ligaments to support the back, owing to fatigue in consequence of the underlying faulty mechanical construction or abnormally close relation of the bony parts. Such decompensation of muscles and ligaments usually occurs between the ages of 30 and 45 and is most frequently observed from 34 to 39 years, when the person is no longer physically as active and hence muscle tone and ligament support are not so effective as in the younger age group.

3. While my experience with compensation cases has not been extensive, I agree with Compere that these patients are best considered for spine fusion after financial settlement has been made, unless there are marked abnormal changes at the lumbosacral junction.

4. Arthrodesis of the spine for low back pain is contraindicated in the emotionally unstable or psychiatric patient, as well as in the elderly person.

605 Commonwealth Avenue.

ABSTRACT OF DISCUSSION

DR. ALLEN F. VOSHELL, Baltimore: I am in accord with the principles given by Dr. Haggart under his conditions and only wish all would as carefully limit themselves as he has done. I wish he had reviewed his ideas on the "compensation back" and applied his fundamentals thereto. Not only is the diagnostic decision exceedingly difficult in this group but more so is treatment whether conservative or operative. The use of the same treatment for a noncompensatory as for a compensatory patient will most times result in an entirely different outcome. Almost all his cases are of the nonindustrial type, which might have some bearing on the speed of recovery and the high percentage of excellent results. I should like to ask whether his four cases of failure to recover and improve were due to non-fusion or to some other reasons. What type of fusion was followed? And over what area? Was the postoperative care

associated closely with muscle building and was physical therapy carefully controlled? If so, for how long?

DR. FREDERICK A. JOSTES, St. Louis: Most orthopedic surgeons who have had the opportunity to fuse lumbosacral joints because of backache have encountered the great difficulty presented by the compensation boards, insurance companies and the like. Some insurance companies have come to the point where they have flat-footedly said that no fusion shall be done in any patient of theirs. That, in my estimation, is a wrong attitude. However, before a radical procedure such as a spinal fusion is offered to a patient, one should offer him adequate conservative treatment, including firm support in the way of a bed and a brace, and his activity at least during that period should be limited. The burden of proof is on the man who sees the patient in his first attack of backache. I am certain that chronicity of back conditions may depend very much on the initial treatment. Such patients should have the usual supportive measures, gentle manipulation and complete rest for at least several days. It is most difficult to get these patients to rest, especially if one has been able promptly to relieve them of acute pain by manipulative procedure. Much time from usual activity and loss of working hours could be avoided in this way and recurrences are less apt to happen. It seems only fair that in selected cases in which extraneous factors such as compensation diseases or escape mechanisms have been definitely ruled out, given a young individual or even an older one who has repeated attacks of pain, repeated loss of time from whatever activity the patient indulges in or one who must so completely limit his activities as to interfere with his normal way of living, even though one can relieve him promptly of his pain in each attack, such persons should be offered the opportunity to be made free from attacks and pain and limitation of activity by a fusion operation. As suggested, compensation cases might be done after a settlement has been made. Promiscuous fusion, of course, is to be condemned.

DR. G. E. HAGGART, Boston: I did not go into the technical aspects of the fusion operation because of limited time. The fusion in these cases was performed on the lumbosacral joint except in patients with spondylolisthesis, where the fourth lumbar vertebra was included. The Hibbs technic, slightly modified, was employed. We do not transplant bone from the tibia as has been done in the past, but we do secure additional bone from the posterior superior iliac spine which can be exposed through the same incision, swung slightly to the side from which the bone is to be taken. The iliac spine is exposed by dissecting free the skin and subcutaneous tissue from over this area; the bone directly underneath is then denuded of soft parts, and it truly offers a "well" from which it is possible to obtain a large amount of soft medullary bone shavings which, when packed about the lumbosacral facets, are extremely helpful in producing rapid fusion. The length of time patients were kept in bed postoperatively was a minimum of six weeks; the average is seven. When the patient had to leave the hospital (via ambulance) for financial reasons or any other factors, he remained in bed at home a minimum of eight weeks. Just before he is allowed up the patient is fitted with a Taylor type back brace. While in bed he has not worn a support but lies on a firm fracture bed. This is much more comfortable than wearing a cast or brace in bed, which I do not think is necessary. When the patient is ambulatory, the Taylor back brace is worn three months on the average. In some instances it has been much shorter. This decision obviously depends on what the post-operative roentgenogram reveals, and we are guided by that together with the general condition of the patient. The point Dr. Voshell brings up about exercises is significant. Obviously, a back will not function simply because one has an internal bone splint. It is also essential to have muscle power. None of these patients were operated on until they had completed a preliminary interval of muscle training, which likewise they carried out after operation. The point I wish to emphasize about this group of individuals in their thirties with low back pain due to an unstable lumbosacral joint is that if they have developed in that age period severe disabling back pain and if a definitive, that is, a limited period of conservative therapy is not successful in relieving symptoms, then I believe the question of a fusion operation should be considered. In my opinion these patients should be advised to have an arthrodesis of the lumbosacral joint.

THE PATHOLOGY AND TREATMENT
OF OBSTRUCTIONS AT THE VESI-
CAL NECK IN WOMENHUGH H. YOUNG, M.D.
BALTIMORE

The pathology and treatment of obstructions at the vesical neck in women and the inflammatory conditions that lead up to them have received scant attention in the American literature. Two years ago I was able to collect and present thirty-six cases. I showed that the development of hesitation, difficulty in starting micturition, slowness of the stream, irritation, pain, hematuria and the presence of more or less complete retention of urine are quite similar to those conditions in men. On cystoscopic examination the mucosa of the urethra and adjacent portion of the trigon is inflamed, often edematous or even papillomatous. The trigon sometimes hypertrophies as a result of the obstruction. The bladder becomes trabeculated and sometimes cellular from back pressure and increased activity of the detrusors. Impairment of renal function may result from residual urine and back pressure effects on the ureteral orifices and the consequent dilatation of the ureters, pelves and thinning of the renal cortex. With

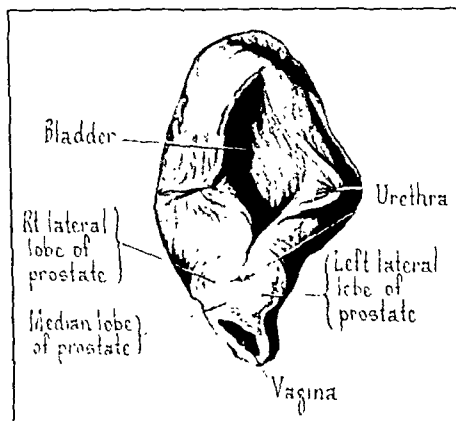


Fig. 1.—Autopsy specimen showing cross section of a prostate of almost normal male dimensions from a female with virilism due to adrenal hyperplasia.

the advent of infection the condition becomes aggravated and ultimately the results may be very serious.

I found that Caulk¹ was apparently the first to report the removal of the obstruction in one of these cases. He employed his cautery modification of my punch instrument. Since then other urologists have employed my simple cold cutting punch, the fulgurating punch of Thompson or the electrical resector of McCarthy. A few operators have attacked the obstruction suprapubically by excision or enucleation. Folsom and others have held that glands which they found in the region of the vesical neck of the female urethra are largely responsible for the persistence of inflammatory conditions and for the development of obstruction. In 1853 Virchow first noted stones in the female urethral glands resembling those found in the male prostate. He concluded that they were homologous structures.

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

Read before the Section on Urology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Caulk, J. R., and Patton, J. F.: The Cautery Punch Operation for the Removal of Obstructive Lesions at the Vesical Orifice in Women and Children. *J. Urol.* 33: 504-512 (May) 1935.

Since then many others have held that certain structures in the female urethra are homologues of the male prostate. Tourneux (1889), Magee (1892), Pallin (1901) and Eratt (1911) reported finding the presence of prostatic homologues in varying amounts along the entire female urethra. Eggerth (1915) pointed out that the anlage of the bulbo-urethral gland (Cowper's gland) and the major vestibular glands (Bartholin's glands) of the human embryo are homologous.

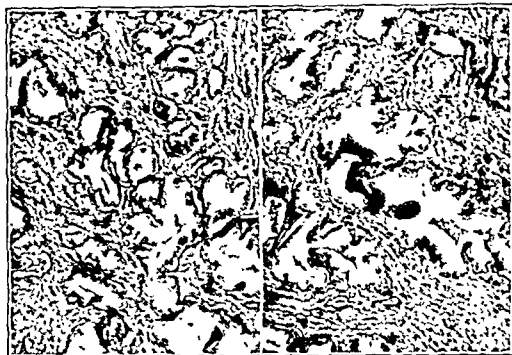


Fig. 2.—Appearance of two sections of a large prostate from a female with adrenal hyperplasia.

In 1922 Johnson,² working in this clinic, made the most exhaustive embryologic study of the vesical neck in the female. He made serial sections of female embryos of various lengths (60, 75, 150, 215 and 275 mm.) and from these prepared wax reconstructions that showed glands along the urethra from the vesical orifice to the meatus which, he asserted, corresponded to the prostatic glands in the male. Johnson asserted positively that "the whole homologue of the prostate in the female was here demonstrated for the first time." Johnson also studied by serial sections the glands of the



Fig. 3.—Section showing glands beneath urethra in vesical neck which correspond to prostatic glands in the male.

adult female urethra and concluded his study with the statement that the urethra in the female corresponded with that portion of the male urethra which lies between the prostatic orifice and the utricle.

Coincidentally with the formation of prostatic glands in the male, similar glands appear in the female. These prostatic glands in the female correspond in number

2. Johnson, F. P.: The Homologue of the Prostate in the Female. *J. Urol.* 8: 13-34 (July) 1922.

and give rise to branches, but they never attain the development of the male prostatic glands except when, as a result of hyperplasia of the adrenal cortex (the androgenic zone), these prostates in females continue their growth and ultimately almost attain the development of the male prostate. In the normal female these glands, according to Johnson, differ from the prostatic glands in being fewer in number, being less closely packed together, having fewer branches and showing much less evidence of active secretion. In "Genital Abnormalities: Hermaphroditism and Related Adrenal Diseases" I³ presented autopsies on three female pseudo-hermaphrodites in which great enlargement of the adrenals was found. In between the cortex and the medulla there was a tremendous development of the androgenic zone of Grollman characterized by the presence of many fuchsinophil cells. In these cases the prostate was considerably developed. The prostate from one of these patients is shown in figure 1. As seen here this patient, a woman of 26, had a prostate of almost normal male proportions. In figure 2 are shown sections of the prostate from another one of these patients. The similarity to the normal male prostate is evident.

At my request Dr. John Haines has secured sections from routine autopsies in the department of pathology. In figures 3 and 4 the typical appearance of these periurethral glands in the female is seen. The important role played by inflammation involving the urethra and the periurethral glands in the female is shown in the following case:

A woman aged 66 was admitted with complete retention of urine of eight months' duration. For a time there had been marked nausea, vomiting and severe uremia. She then began a catheter life and when she came to us her bladder was being emptied four times a day. Cystoscopy showed a contracted vesical neck with a posterior bar that was identical in appearance with that frequently seen in the male. The trigon was hypertrophied and the bladder was trabeculated and held 500 cc. of residual urine. With my cold cutting punch the obstruction was removed in three cuts. The patient left the hospital able to void normally and has now been followed for nine years.

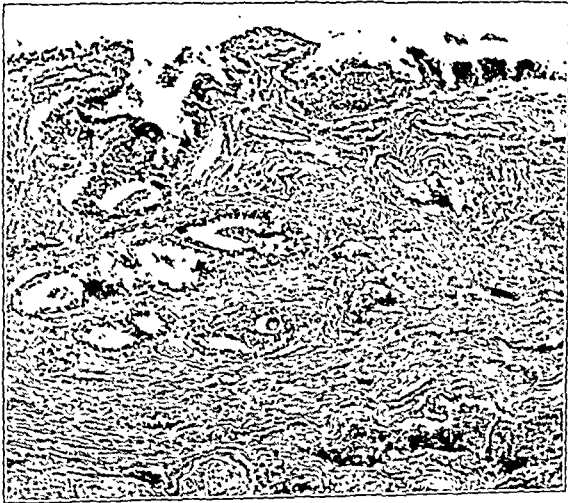


Fig. 4.—Section showing suburethral glands near vesical neck, homologues of prostatic glands in the male.

The operative result is considered perfect. Photomicrographs of the tissue removed by the punch instrument in this case are reproduced in figures 5 and 6. As seen here, considerable inflammation of the periurethral glands in the formation of marked fibrosis is present.

3. Young, H. H.: *Genital Abnormalities: Hermaphroditism and Related Adrenal Diseases*, Baltimore, Williams & Wilkins Company, 1937.

This case is somewhat similar to others that we have studied. In most instances the obstruction has not been so complete or the gradual development so pronounced. In some much more fibrosis is present. In all it seemed evident that chronic inflammation played an important part in the case. We have in our files the

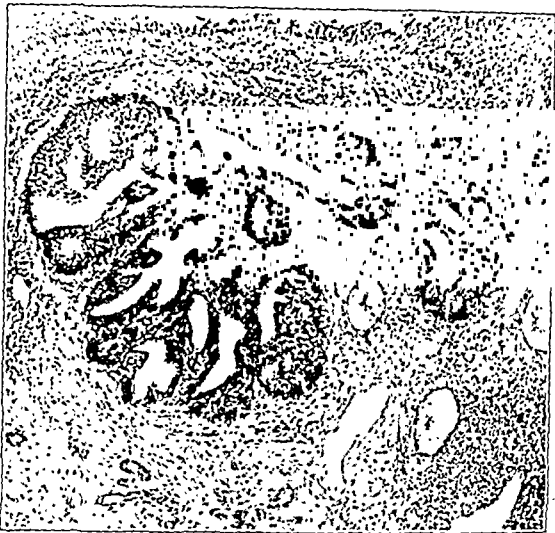


Fig. 5.—Section of tissue removed by punch operation on a woman with obstruction to urination (complete retention). Glands homologous to prostate surrounded by chronic inflammation and bar formation are seen.

case histories of some 500 women suffering with inflammatory conditions varying in degree at the vesical neck and the adjacent portion of the urethra. The

Symptoms of Chronic Urethritis (Nonspecific) in Women
(101 Cases)

	Cases
Frequency	78
Burning	31
Urgency	26
Backache	24
Hematuria	16
Pain in renal region	15
Suprapubic pain	20
Painful urination	15
Bearing down feeling	13
Pain in bladder	9
Difficulty or hesitancy in voiding	9
Incontinence	7
Straining on urination	2
Cloudy urine	1
Bladder tenesmus	1
Leukorrhea	1
Painful coitus	1

symptoms noted in the 101 cases studied in detail are given in the accompanying table.

On cystoscopic examination with the right angle telescope one sees only the conditions within the bladder at the vesical orifice. In the presence of a contracture or a bar, either posterior (fig. 7) or anterior, the condition is easily seen with this type of telescope. For lesions farther out in the urethra my antegrade telescope or the fore-oblique telescope of McCarthy is essential. With these instruments one sees all degrees of inflammatory change from simple urethritis to edema, irregular swellings of the mucous membrane, definite cysts and polypoid growths of varying degree (fig. 8). Rarely ulceration is present. The entire urethra generally shows a marked reddening and evidence of chronic inflammation. With the instrument in the urethra and a finger in the vagina, thickening of the urethra, par-

ticularly at the vesical neck, is often demonstrable. In some cases a definite stricture is present. Caruncles are not infrequently seen at the urethral meatus.

These cases present a common and often very troublesome condition in women that is often overlooked. The fact that the urine is usually normal, the cultures grow no bacteria and the ordinary cystoscope shows a vesical orifice that appears normal with the right angle telescope has led many observers to pronounce the urethra normal and to seek to relieve these patients by ureteral instrumentation. This is particularly true when pain in the back with attacks of colic in the region of one or both kidneys strongly suggests ureteral and renal abnormality. Benefit following cystoscopy and ureteral dilation not infrequently has been accepted as confirming the diagnosis, but such benefit may indeed be the result of urethral instrumentation rather than ureteral. As shown in 101 cases analyzed, the symptoms are apparently localized quite a distance from the urethra. It is therefore highly essential that, even when the history of the patient seems to point strongly to disease of the upper urinary tract, a very careful study of the urethra should be made, and if evidence of chronic inflammation and the various pathologic conditions described are present local treatment for the urethra and vesical neck is indicated, certainly as a preliminary measure before the patient is subjected to a series of ureteral dilations or operations on the kidney itself.

CONCLUSIONS

Chronic inflammatory conditions in the female urethra, especially in the deep portions and at the vesical neck, are common in women. They are accompanied by symptoms that are often referred to regions higher up in the urinary tract. In most cases, however, local symptoms are present in the urethra and bladder. Chronic inflammatory changes in the mucous membrane, in periurethral structures and particularly in the glands are often present and evinced by swelling, by edema, by cystic and polypoid formations and sometimes



Fig. 6.—Section showing fibrosis at vesical neck and submucous glands homologous to prostate.

by the development of definite bars or contractures of the vesical orifice. For the proper study of these cases an antegrade or fore-oblique telescope or urethroscope is essential. These lesions may often be missed during the course of cystoscopy with the right angle telescope. The conditions which produce such severe

local and referred symptoms are readily cured by endo-urethral treatment: applications of silver nitrate, fulguration, the punch operation or excision of the obstructing bar, or severely inflamed regions either with the simple punch instrument or the electrical resectoscope. Care must be taken not to overdo lest



Fig. 7.

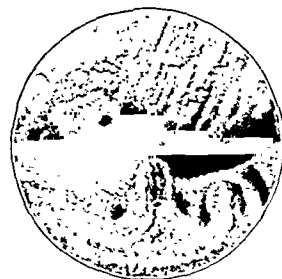


Fig. 8.

Fig. 7.—Cystoscopic view of rounded bar at vesical neck of a woman which caused marked obstruction to urination.

Fig. 8.—Urethral polyps just below vesical neck due to chronic inflammation. These are easily destroyed by fulguration or simply by applications of silver nitrate stick.

incontinence for a time may occur. Accurate and adequate endoscopic methods often clear up these long standing and troublesome conditions.

ABSTRACT OF DISCUSSION

DR. HENRY DAWSON FURNESS, New York: I have been familiar with the work on the glands of the urethra; a German some years ago reported that he had found in some of these glands corpora amylacea. However, I don't believe I have seen exactly the kind of cases that Dr. Young reports. I have seen many cases of urethral obstruction with the retention and pathologic condition of the upper urinary tract; also patients with residual urine which I thought was more apt to be due to some cord lesion than to any obstructive lesion in the urethra itself. I see a few cases of urethral stricture, but even with those with rather marked obstruction I do not see much evidence of retention or urinary tract infection. Dr. Emmet, of the Mayo Clinic, recently brought out that in many of these cases retention of urine is due to a disproportion of the expulsive force of the bladder and the retentive force of the sphincter; that when the retentive force is disproportionately greater than the expulsive force there is retention and residual urine. I shall be on the lookout for the type Dr. Young has described. My experience has been mostly that in cases of retention there are cord lesions.

DR. ALF. F. GUNDERSON, La Crosse, Wis.: Dr. Young has called attention to an important condition which the average urologist rarely has occasion to see. The total number of reported cases of true intrinsic bladder neck obstruction in the female numbers only about 50 cases. The diagnosis is not difficult but one must exclude (1) gynecologic conditions such as uterine tumors and cystocele, (2) intra-urethral pathologic conditions—strictures, urethral diverticula, polyps, (3) intravesicular tumors and (4) hysteria. After exclusion of these factors one is aided by cystoscopy. Observers write about a bar, a ridge, fibrous contracture, hypertrophy of the internal sphincter that one can easily see through a cystoscope. I am impressed with the paucity of actual visible abnormality in the bladder neck in such cases. I would sound a note of warning! The female sphincter as seen through a urethroscope is often deceiving and gives one the impression of being the seat of a bar or contraction. One should attach greater importance to evidence of obstruction as found in the bladder—residual urine, trabeculation, saccules—rather than the appearance of the bladder neck. The amount of tissue present as an obstructing factor is truly disappointing. There is no uniformity of opinion with regard to the causation. Infection with resultant fibrosis and contracture with occasional hyperplastic glandular structures has been the generally accepted course of pathologic events. This theory was advocated by Caulk, Folsom, Van Houton and

others. However, Braasch and Thompson have been unable to demonstrate a greater amount of fibrosis in the removed tissue than there is present in the normal female bladder neck at necropsy. A greater amount of inflammatory cells has been seen as well as some hypertrophy of the epithelium and muscle bands. These observers feel that the inflammation, although the exciting cause, does not adequately explain the true basic etiology. They suggest an associated neurogenic cause: a nervous unbalance between the sphincteric musculature and the detrusor muscle which leads to a spasm of the sphincter, and subsequently to hypertrophy, and, finally, occasionally to active hyperplasia of the muscle. More evidence has accumulated to support this hypothesis by recent information obtained in the treatment of the neurogenic bladder or tabetic bladder by resection of the internal sphincter. Emmet in a recent publication has brought this forcibly to our attention. Resection of the sphincter as advocated by Caulk, Thompson, Emmet and others is merely an effort to facilitate emptying of the bladder by weakening one muscle against another or creating a more favorable muscle balance or readjustment.

DR. EDWARD N. COOK, Rochester, Minn.: The paucity of evidence that we see on cysto-urethroscopic examination around the bladder neck is the most interesting part to me of this problem. We must depend on our history concerning obstructive difficulty, small stream, frequent passage of the urine and occasionally the association of burning, the presence of residual urine and the appearance on cystoscopic examination, not at the bladder neck but rather in the bladder itself, such as trabeculation and cellulæ formation. This condition is worthy of our very careful consideration. It is true that not many cases have been reported. Thompson reported 24 at the Quebec meeting. We have had 12 cases since that time. Of interest is the fact that in most cases only a small amount of tissue will need to be removed. Occasionally one or two bites or nothing more than a sphincterotomy at times will relieve these patients of their symptoms. They are a group which have been treated unsatisfactorily for a long while, and I think we should pay more attention to them. As regards the pathologic conditions found I have not been particularly impressed with the amount of fibrosis and have not felt that this could be attributed to an inflammatory process; first, because of the fact that the inflammatory process in the female urethra is notoriously a frequent occurrence and yet obstruction in the female urethra is notoriously rare. Second, if one will examine the tissue removed in these cases and also examine postmortem tissue from the urethra in females that never had any difficulty with urination one will see little or no difference. It is possible that hypertrophy of the sphincter muscle as a result of spasm is the most common cause of the condition. In some cases a neurogenic dysfunction has led to sphincteric hypertrophy in my opinion.

DR. T. LEON HOWARD, Denver: If Dr. Folsom were here he would greatly appreciate the fact that Dr. Young has substantiated his observations, for he has insisted for many years that these are true glands and that they are often infected. Dr. Young's sections have proved that this is a fact. It seems to me that I see these patients every day. Others see them too, but if one is attempting to view the urethra and bladder sphincter with an ordinary Brown-Buerger cystoscope one is passing over the pathologic condition. If there is a disease condition present and one uses a fore-oblique lens cystoscope, there will be no difficulty in locating it and opening or destroying the polypoid-like growths with a fulgurating wire. This condition often begins during childhood, and patients go through life suffering from its effects. Pyelitis in children is frequently the result of infected glands in the posterior urethra, and until one cures these glands one cannot cure the pyelitis. Many pediatricians have failed to recognize this. It is astounding how many females have residual urine caused by these obstructing polypoid growths. If you suspect that they have residual urine and want to prove it easily, put ordinary liquid petrolatum in the bladder. If there is residual urine you will find liquid petrolatum floating on top of the next catheterized specimen whether it is obtained at the end of a week or a year. There is no guesswork about this test in either the male or the female patient.

DR. HUGH H. YOUNG, Baltimore: I have purposely not discussed cases in which there were spinal cord and other neurologic lesions present. These cases belong to a separate group. With proper urologic methods, including cystometric studies, they can be differentiated from the inflammatory and obstructive conditions to which I have limited my paper. Dr. Howard has emphasized the fact that with the ordinary cystoscope many of these conditions at the vesical neck in women are missed. My antegrade telescope or McCarthy's fore-oblique will show very well these changes at the vesical neck and in the deep urethra in women. They are indeed quite common and are responsible for many referred pains as well as many errors in diagnosis. I saw a woman recently who came because she had seizures of severe pain in the vesical neck. The ureters had been dilated many times; she had received orthopedic treatment, bladder lavage and stretching without relief. I found pronounced inflammatory conditions at the vesical neck with a little obstructive bar and much glandular inflammation. A small punch operation and treatment of the posterior urethritis with silver nitrate cured her completely. Another woman with very severe bladder and back pains had a large polyp and other inflammatory conditions deep in the posterior urethra and vesical neck. She had become a morphine habitué as a result of years of suffering. Local treatment relieved her. My simple tubular endoscope with application of silver nitrate, either by means of the stick or by means of 20 per cent solution on swabs, is usually entirely effective. Too much deep resection or fulguration is not advisable. When there is definite obstruction, the resection which I have described is very effective.

DIASTASIS OF THE DISTAL TIBIOFIBULAR JOINT AND ASSOCIATED LESIONS

RUFUS H. ALLDREDGE, M.D.

NEW ORLEANS

Diastasis of the distal tibiofibular joint is associated with extensive ligamentous rupture and results from external rotation or abduction injuries at the ankle. It may occur without associated fracture but is more frequently seen in cases of Pott's fracture in which there is fracture of the internal malleolus or rupture of the internal lateral ligament together with fracture of the lower third of the fibula. There may also be a fracture of the posterior aspect of the tibia extending into the joint.

Most articles in the literature on fractures of the ankle with rare exceptions¹ direct attention to the fractures of the malleoli and posterior tibial margin, leaving the impression that diastasis is of secondary importance. Undoubtedly failure to recognize and treat properly the diastasis may result in permanent disability even when the associated fractures are accurately reduced.

An effort has been made in this presentation to call attention to some practical points of importance regarding rupture of the distal tibiofibular ligaments and the associated injuries.

ANATOMY AND PHYSIOLOGY OF THE TIBIOFIBULAR JOINT

It is necessary here to review briefly the anatomic structures of the ankle joint which have direct bearing on the subject under consideration.

From the Department of Surgery, Division of Orthopedic Surgery, Tulane University of Louisiana School of Medicine and Charity Hospital and Touro Infirmary.

Read before the joint meeting of the Section on Surgery, General and Abdominal, and the Section on Orthopedic Surgery at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Merle d'Aubigné, R., and Smets, W.: Les formes frustes de déplacement externe de l'astragale dans les fractures malléolaires, *Presse méd.* 42: 157, 1934. Apfelbach and Boim.²

There is a definite but atypical articulation between the distal tibia and fibula, and the synovial membrane usually extends up between these two bones for a distance of about one-fourth inch.



Fig. 1.—End result of unrecognized and untreated tibiofibular diastasis compared to the normal ankle. Note osteo-arthritis and narrowing of joint space. Ankle fusion was necessitated by complete disability.

The distal ends of the tibia and fibula are bound together by rather weak ligaments. These ligaments are (1) the anterior lateral malleolar (anterior inferior tibiofibular ligament), (2) the posterior lateral malleolar ligament (posterior inferior tibiofibular ligament), (3) the transverse ligament, which is an extension of the posterior lateral malleolar ligament, and (4) the interosseous ligament, which is a direct extension of the interosseous membrane extending downward to the

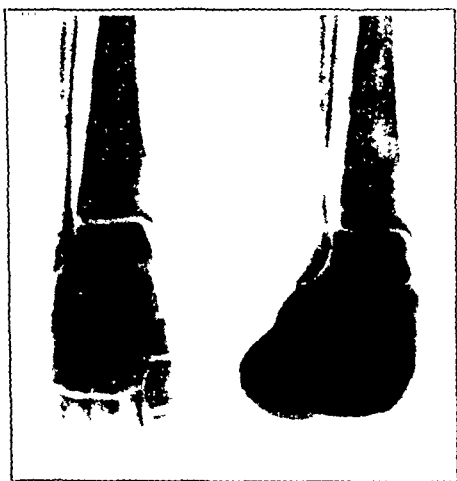


Fig. 2.—Normal amount of separation of fibula from tibia when foot is dorsiflexed. Left, plantar flexion. Right, dorsiflexion. Note difference in width of tibiofibular joint space.

synovial cavity. The latter is longer in front than behind and occupies the space between the anterior and posterior malleolar ligaments.

Because the astragalus is 25 per cent wider in front than behind, it is necessary for fibular motion of some

type to take place at the ankle mortise when the foot is dorsiflexed, even though the mortise is also slightly wider in front than behind. Just what these motions are has not been clearly described. It has been said² that the fibula glides upward on its long axis when the foot is dorsiflexed and downward when it is plantarflexed. Efforts in this study to confirm this view have been unsuccessful. Measurements of x-ray films taken on the normal proximal and distal ends of the fibula do not show any movement in its long axis on extreme motions of the foot. It must be concluded, therefore, that the fibula does not glide upward or downward in its long axis.

It has been shown by taking anteroposterior x-ray films on the normal ankle that definite widening of at least 2 to 3 mm. takes place at the tibiofibular joint when the foot is dorsiflexed. Slight anteroposterior motion of the fibula has also been demonstrated at the lower tibiofibular joint by inspection of the fresh specimen. When the tibiofibular ligaments are sectioned, the fibula separates abnormally from the tibia when on dorsiflexion the foot reaches 90 degrees. The clinical importance of this fact will be indicated later.

DIAGNOSIS OF TIBIO-FIBULAR DIASTASIS

Clinical signs and symptoms of rupture of the ligaments and diastasis of the tibiofibular joint depend on the extent of injury and whether associated fracture is present. Frequently, when associated with a Pott's fracture, the signs and symptoms of the fracture completely overshadow those of tibiofibular ligament rupture and diastasis. Swelling and tenderness over the distal tibiofibular joint may be indicative when the fracture of the fibula is fairly high. This sign is of no value when the external malleolus is fractured. Gross ballottment of the fibula may rarely be present. Widening of the malleoli and abnormal anterior and posterior motions of the fibula may be seen when the ligaments are extensively torn.

Proper x-ray examination is important in every case. The preliminary use of local anesthesia may facilitate the taking of proper views. The x-ray examination should be considered as an adjunct in diagnosis and the surgeon should, if possible, be present when the x-ray films are made so that proper views will be assured. All anteroposterior views of the ankle joint should be taken with the malleoli equidistant from the x-ray film. The following views should be taken in all doubtful cases: (1) anteroposterior with the foot plantarflexed; (2) anteroposterior with the foot dorsiflexed; (3) anteroposterior view with the foot in external rotation; (4) lateral view with the foot in neutral position. If the usual anteroposterior and lateral views show dis-

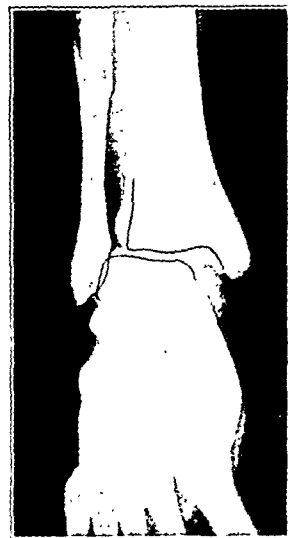


Fig. 3.—Gross tibiofibular diastasis. Note abnormal width of joint space between internal malleolus and astragalus, loss of parallelism of joint lines of lower tibia and astragalus, and lateral displacement of astragalus.

2. Apfelbach, George, and Boim, Leon: Fractures of the Ankle. Arch. Surg. 35: 328-357 (Aug.) 1937.

tinctly the exact nature of the lesion and especially if gross diastasis is present in these views, the others may be omitted. Fluoroscopic examination is probably not as accurate as the examination of carefully taken x-ray films in the various positions.

A thorough understanding of the mechanism of fractures about the ankle is a prerequisite to proper interpretation of the x-ray films. It should be kept in mind that extensive ligamentous injury is as important as bony injury and may be diagnosed from the x-ray films alone.

The presence of an isolated fragment of bone between the distal tibia and fibula is a positive sign of diastasis and results from ligamentous avulsion of the outer border of the tibia. Rupture of the tibiofibular ligaments with diastasis is present in most cases in which there is a fracture 2 or 3 inches above the lower tip of the fibula associated with fracture of the internal malleolus or rupture of the internal lateral ligament.

Widening of the space between the internal malleolus and the internal aspect of the astragalus when the

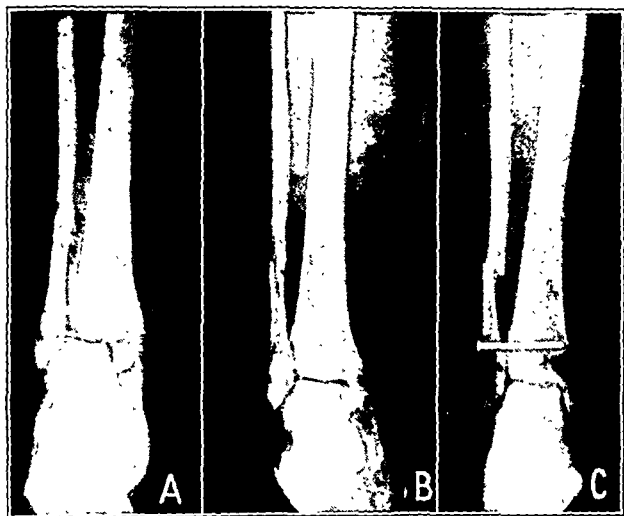


Fig. 4.—A, note in addition to all signs indicating tibiofibular diastasis the fragment of bone avulsed from the lateral aspect of the tibia. B, same case after attempted closed reduction. Loose fragment of bone became interposed between the fibula and the tibia. C, same case after operative removal of loose fragment and fixation of fibula to tibia by means of a vitallium screw. Note accuracy of reduction of internal malleolus. It reduced spontaneously when the fibula was approximated to the tibia.

internal malleolus is not fractured indicates both a rupture of the internal lateral ligament and tibiofibular diastasis when the fibula fracture is fairly high.

Normally the external border of the astragalus is in line with the external line of the tibia and any deviation of this normal alinement to the lateral side indicates lateral displacement of the astragalus. Diastasis is a frequent cause of lateral displacement of the astragalus.

In the normal ankle the joint lines between the lower tibia and the superior border of the astragalus are parallel. Diastasis with lateral displacement of the astragalus is a frequent cause of loss of parallelism of these lines. Fracture of the internal and external malleolus or rupture of the internal lateral ligament are other causes of loss of parallelism of the joint lines.

Gross diastasis of the mortise with marked widening between the tibia and the fibula are usually recognized without difficulty. Complete diastasis with interposition of the talus is rare and occurs only when the ligaments and interosseous membrane are completely torn. In

doubtful cases x-ray films of the normal ankle in plantar flexion and dorsiflexion compared with those of the injured ankle may be of aid. The normal amount of widening when the foot is dorsiflexed should be kept in mind.

TREATMENT

Treatment of rupture of the tibiofibular ligaments and diastasis should be based on anatomic and physiologic considerations, taking into account the normal motions at the tibiofibular joint. The importance of early recognition and treatment cannot be overestimated. Apfelbach and Boim² in 300 films of ankle fractures noted diastasis in 40 per cent at the time of injury, whereas widening of the mortise was observed in 94 per cent as a clinical end result.

It must be kept in mind that not only widening of the ankle mortise but anteroposterior instability of the distal end of the fibula may result if diastasis is not recognized and properly treated. If normal motions and ankle joint stability are to be preserved, early accurate reduction must be carried out and maintained until the ligaments and the associated fractures have healed.

In the presence of definite tibiofibular diastasis the tibia and fibula may be reapproximated readily, pro-

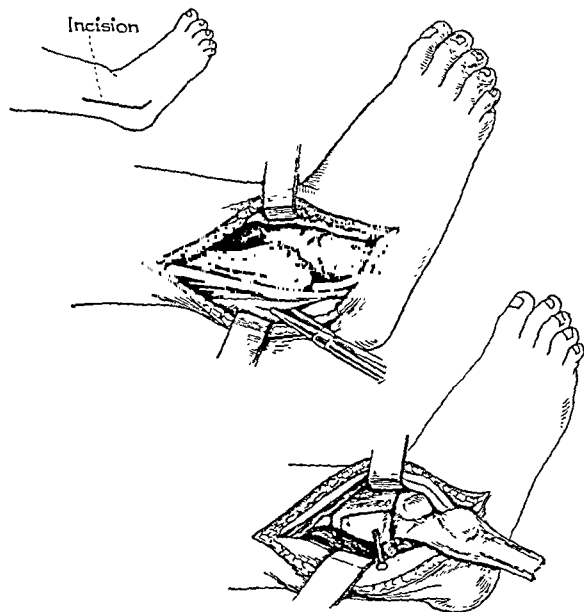


Fig. 6.—Gatellier's approach to posterior tibial marginal fracture. Indicated when closed reduction is unsuccessful and when there is complete rupture of the tibiofibular ligaments. In addition, the internal malleolus may be approached through a separate medial incision if necessary.

vided there is no interposition of soft tissue or bone. When difficulty is encountered in effecting reduction, interposition is usually found to be the cause. Organized clot may give the same effect in late cases. Operation should be resorted to without hesitation under these

circumstances and the interposed substance removed or accurately replaced. The approach is made through a short incision over the anterior aspect of the tibiofibular joint. If difficulty is encountered in holding the fibula in its place well against the tibia, a screw or wire may be inserted through a small incision on the lateral aspect of the fibula.

The question of the routine use of metal fixation of the fibula to the tibia is one that has not been definitely settled. Undoubtedly it may facilitate the handling of these cases in some instances. One may cause fractures of the internal malleolus with gross displacement to reassume readily the normal relation to the tibia simply by reducing the diastasis and adequately maintaining reduction by the use of a screw. Removal of the metal fixation should be carried out in every case as soon as the ruptured ligaments have healed. Failure to do so usually results in the loss of dorsiflexion because motions of the fibula are prevented when it is fixed to the tibia.

The position in which the foot is immobilized after reduction has been effected is of importance whether internal fixation is used or not. It has already been brought out in this study that separation of the mortise after the ligaments are divided takes place when on

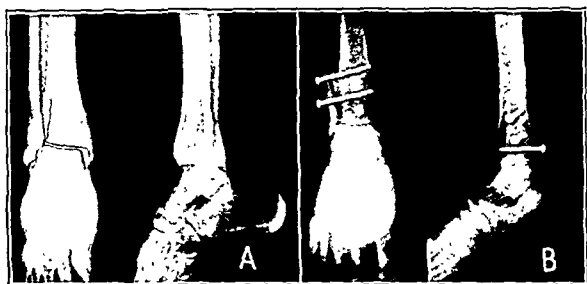


Fig. 7.—A, tibiofibular diastasis, fracture in the lower fourth of the fibula, fracture of internal malleolus and posterior tibial marginal fracture. Closed reduction unsuccessful. B, after operation. Gatellier's approach used. Tibiofibular screws should always be removed when union has occurred.

dorsiflexion the foot reaches 90 degrees. The position of choice for postreduction immobilization then is slight plantar flexion, the position which eliminates any tendency for separation of the two bones. This should also be kept in mind in cases in which there is a posterior marginal fracture of the tibia, as the usual position of fixation in dorsiflexion may at the same time cause separation of the fibula from the tibia.

In certain cases of diastasis associated with Pott's fracture and posterior tibial marginal fracture in which the fibula is broken two or three inches above the ankle joint, Gatellier's³ approach has been found to be very satisfactory. This method is used when, for some reason or other, the posterior tibial fragment cannot be brought down into normal position. A lateral peroneal approach is made and the peroneal tendon retracted forward. The distal end of the fibula is freed and reflected downward, the external lateral ligaments acting as a hinge. The posterior tibial fragment is accurately reduced and fixed with screws. The fibula is then replaced and fixed with screws and the peroneal tendons are brought back into their normal positions.

3445 Prytania Street.

3. Gatellier, Jean: The Juxta-retroperoneal Route in the Operative Treatment of Fracture of the Malleolus with Posterior Marginal Fracture, *Surg., Gynec. & Obst.* 52: 67-70, 1931.

ABSTRACT OF DISCUSSION

DR. CLAY RAY MURRAY, New York: Dr. Alldredge's paper has presented clearly a frequent problem in ankle fractures which is often overlooked with resultant disability. Disruption of the inferior tibiofibular joint is a common complication of high fractures of the lower fibula and a frequent enough complication of other ankle fractures. It is usually a far more serious lesion than any of the associated fractures from the standpoint of difficulty of treatment as well as resultant disability. Treatment of it does not enter into consideration in many cases because its presence is not recognized. Often the discovery of a widened mortise, an unstable ankle and a secondarily stiff and painful joint due to traumatic arthritis is made in a follow-up examination many months after the original injury. He has outlined clearly the important points in the diagnosis of this condition. It should be looked for and eliminated as a possibility in all ankle fractures before treatment for the fracture is instituted. Its common occurrence is one of the best arguments I know of against the marked inversion of the foot so commonly practiced in the immobilization of ankle fractures, since it is with marked inversion or eversion of the foot that x-ray examination most clearly demonstrates the diastasis of the tibiofibular joint. With proper x-ray examination using, as Dr. Alldredge suggests, a position (among others) which gives an anteroposterior view of the ankle with the foot in eversion or pronation (Dr. Alldredge refers to it as external rotation), the diastasis when present can be clearly shown. Marked inversion or supination of the foot will produce the same result. It is obvious then that any marked eversion or inversion of the foot as a position of fixation is a sure way to maintain the diastasis. When reduction is delayed in these cases, clotting of hemorrhage and exudate in the widened joint space may prevent reduction by closed methods, and interposition of ligamentous tissue or bone fragments may have the same effect. Failure to correct the diastasis is revealed in the postreduction x-ray films if they are taken in accordance with the directions given in Dr. Alldredge's paper. In the event of such failure, operative measures are indicated. When no such interposition exists, which is in the majority of cases, the reduction must, in addition to replacing bone fragments, firmly compress tibia against fibula at the tibiofibular joint, and the fixation must maintain this compression not only until such time as the ligaments have healed but until the healing has become strong enough to stand the strain of dorsiflexion of the foot. Where the diastasis has been rather easily recognized, full weight bearing on these ankles, even though the x-ray films may appear perfectly satisfactory, should be delayed for from twelve to sixteen weeks from the time of injury.

DR. GEORGE O. EATON, Baltimore: Dr. Alldredge is to be congratulated on emphasizing the presence and the importance of a tibiofibular diastasis. There is one point that I feel like complaining about. Dr. Alldredge states that fluoroscopic examination of the ankle is probably not as accurate as x-ray films. I think this is an understatement of fact. I think it is a deplorable habit to depend on fluoroscopic examinations as the x-ray diagnosis of fractures. If a fracture is present one should have x-ray films not only as a permanent record but also as a guide in attacking the problem of reducing the fracture. If the injury to the ankle is a fracture or a fracture without displacement, more often than not it will be missed if dependence is placed on fluoroscopic examination. As regards the posterior tibial marginal fracture, by far the majority of these marginal fractures are less than 30 per cent of the tibial plafond, and conservative treatment in addition to the reduction of the other fractures present can be depended on to yield a good result. Dr. Alldredge's paper is certainly excellent and timely and the literature, as he stated, is scarce on this important subject.

DR. RUFUS H. ALLDREDGE, New Orleans: I tried to stress the treatment of these ankle joint injuries with especial reference to the normal physiologic motions of the fibula. I have also tried to summarize the diagnostic points. As far as the use of the fluoroscope is concerned, in contrast to examination of

carefully taken x-ray films, I can only say that I think in most cases one can make a diagnosis from the x-ray film if one knows what to look for in the way of abnormalities. In posterior marginal fracture of the tibia, unless it is large enough to cause disturbance in function later or unless it is associated with fracture of the lower third of the fibula, together with rupture of the tibiofibular ligaments, it is not necessary to use the radical approach as it can be exposed simply through a posterior incision on the medial aspect of the achilles tendon.

MILKERS' NODULES

FREDERIC T. BECKER, M.D.

DULUTH, MINN.

The opportunity to observe and study four cases of milkers' nodules during the summer of 1939, and my inability to find in the American literature any description of this disease, prompt this report. This is an occupational infection of milkers which may be widely distributed among the dairying communities of our country. It is my purpose to give a clinical description of milkers' nodules and differentiate this disorder from other diseases occurring on the hands of milkers, and discuss the cause, pathology and immunology.

The initial lesions may vary from one to forty in number and they are usually located on the hands and fingers. The incubation period is from five to seven days after contact with a diseased cow, and the infection enters the human skin through abrasions. At the onset an erythematous papule develops, which slowly increases in size, becoming a firm, elastic, bluish red nodule from 1 to 2 cm. in diameter. The lesions may be surrounded by an inflammatory areola and may be found in various stages of development. The nodule becomes semiglobular with a central depression; the surface becomes flat, and when the grayish loose epidermal covering is removed a reddened, granulating base remains. The nodule itself gives rise to few subjective symptoms, only slight pain and mild itching. As healing progresses the entire nodule flattens and the granulation tissue is absorbed; involution becomes complete in from four to six weeks without scar formation. The regional glands are occasionally enlarged and secondary pyogenic infection with lymphangitis may occur. There is little constitutional reaction except in unusual instances, when the eruption becomes generalized or secondary infection ensues.

According to Kummer¹ there have been twelve reports in which a generalized eruption has occurred. These disseminated lesions are multiform in type, being either umbilicated papules, urticarial wheals or macules, any of which may become vesicular or hemorrhagic. This generalized outbreak subsides within a week, and the eruption has been considered as being either toxic or produced by hematogenous dissemination of the infection.

All cases of milkers' nodules have occurred in people employed as milkers of cows on whose udders crusted or ulcerated lesions were found to be present. All cases have developed in the latter part of the summer. One

attack apparently leaves immunity, since we have been unable to ascertain any instance of a recurrence. Most veterinarians have diagnosed the lesions which were present on the cows as being similar to those of cowpox.

DIFFERENTIAL DIAGNOSIS

European investigators differentiate milkers' nodules from other conditions many of which would seldom offer confusion in this country. Symmetrical tylosa of Arzt² consists of bilateral calluses located on the knuckles of both thumbs in persons using the Swiss method of milking. Jadassohn³ described inflammatory nodules which are produced by cow hair entering calluses or fissures. Continental authors also consider hoof and mouth disease in differentiation, but the absence of oral lesions and systemic reaction in milkers' nodules should be sufficient to avoid confusion. In exceptional cases, when the eruption becomes generalized, erythema multiforme might be considered. I considered pyogenic granuloma when I saw my first case, but history of contact with an infected cow, the spontaneous resolution of the nodule, and microscopic examination were diagnostic criteria. The relation to vaccinia will be discussed with the consideration of the cause.

ETIOLOGY AND REVIEW OF THE LITERATURE

The majority of investigators think a virus is the infectious agent. Its relation to cowpox has led to much controversy. Winternitz,⁴ who described the first case of milkers' nodules in 1899, was uncertain about the cause. Frieboes⁵ in 1914 reported a case and inoculated the material into a scarified rabbit's cornea with negative results. He supported cowpox as the cause because the cattle which had been the source of the infection were considered to have this disease by the veterinarians. Paschen⁶ made an extensive review of the literature and was of the opinion that cowpox and milkers' nodules could be sharply separated. He stated that in a disease caused by a pox virus a positive Paul's⁷ test⁸ should be obtained and in all individuals who were infected, either human beings or experimental animals, should be immune to later vaccination with vaccine virus. He was unable to come to any definite conclusion but suggested that the disease was a result of an infection of milkers with vaccine virus which was attenuated by a secondary invader.

Schultze, Seifried, and Schaaf⁹ were among the first investigators able to demonstrate experimentally any relation to vaccinia. They studied twenty cases in various stages of development and by inoculating material from the nodules into calves were able to produce lesions similar to cowpox. Their experimental animals as well as the human patients proved resistant to vaccination with cowpox and reinoculation with a filtrate from

2. Arzt, Leopold: Ueber Berufserkrankungen bei Melkern. Wien. klin. Wchnschr. 37: 630, 1924.

3. Jadassohn, Josef, cited by Paschen.⁶

4. Winternitz, R.: Knotenbildungen bei Melkerinnen. Arch. f. Dermat. u. Syph. 49: 195, 1899.

5. Frieboes, W.: Ueber sogenannte Melkerknoten. Dermat. Ztschr. 21: 310, 1914.

6. Paschen, Ernst: Melkerknoten, in Jadassohn, Josef: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 251.

7. Paschen, Ernst: Der Paulsche Versuch, in Jadassohn, Josef: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 169.

8. Paul found that material from lesions of smallpox and vaccinia when inoculated into a rabbit's cornea produced a keratitis which was plainly visible when the eye was immersed in sublimated alcohol. Microscopic sections of this material revealed gram-negative inclusion bodies (Guarnieri) in the epithelial cells.

9. Schultze, W.; Seifried, O., and Schaaf, J.: Die Melkerknoten und ihre Aetologie. Ztschr. f. Infektionskr. d. Haustiere 31: 295, 1927.

From the Duluth Clinic.

Read before the Section on Dermatology and Syphilology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Kummer, L.: Melkerknoten, in Arzt, Leopold, and Zieler, Karl: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1934, pts. 11-12, vol. 3.

milkers' nodules. These workers also obtained positive Paul's tests in which they demonstrated Guarnieri bodies and they believed that the repeated trauma associated with the occupation of milking favored the development of nodules in some persons rather than the typical vesicopustules of vaccinia.

Stark and his co-workers¹⁰ published an account of experimental and clinical investigation of an epidemic occurring in packing house workers who handled sheep. After repeated animal transfers they were able to produce pox lesions in which they could demonstrate inclusion bodies. These authors believed that their observations spoke for the identity of the virus of milkers' nodules with that of variola vaccine, the former undergoing alteration in its biologic properties by parasitism in foreign hosts, the original properties being recovered by repeated animal transfers.

Gottron¹¹ vaccinated a cow with material from a nodule and produced a papulopustular eruption which was indistinguishable from cowpox; however, he obtained a reinfection in the same animal with pox virus eight weeks later. Tappeiner¹² in his case obtained a positive Paul's test in which Guarnieri bodies could be demonstrated, but the reaction took five days instead of the usual two. He and Gottron were of the opinion that the virus of milkers' nodules was less virulent than that of cowpox.

Many of the recent workers have considered the paravaccine of Lipschutz¹³ as the etiologic agent. Lipschutz found that some people when vaccinated develop a dark red papule instead of the usual vesicopustular reaction. In these lesions he was able to find gram negative inclusion bodies. The infection could be transmitted to animals and human beings but those infected showed no immunity to vaccinia. He also found the virus both of vaccinia and of paravaccinia present in the same calf lymph; the latter, however, did not produce a positive Paul reaction. The microscopic and immunologic studies in paravaccinia as described by Lipschutz resemble those found in milkers' nodules.

Dolgov and Morosov,¹⁴ Zenin,¹⁵ Falchi¹⁶ and Bonnevie,¹⁷ after reviewing the literature and studying their cases, considered the cause of milkers' nodules to be a virus similar to variola vaccine and believe "paravaccine of Lipschutz" the most likely. They based their conclusion on the variation in the pathology of variola and milkers' nodules, the lack of immunity to vaccination with cowpox, and the absence of pustulation in milkers' nodules, which healed spontaneously without scar formation.

Groth,¹⁸ Kaiser and Gherardini¹⁹ and Woringe²⁰ stated that they were unable to make any definite

conclusions as the result of their observations, but they found little evidence to favor vaccine virus as a cause of milkers' nodules.

Histologic interpretations of biopsy specimens of milkers' nodules depend on the age of the lesions. Schultze, Seifried and Schaaf, Woringe and Bonnevie found that in an early lesion there was acanthosis and reticular degeneration²¹ of the upper cells of the malpighian layer with formation of microscopic multilocular vesicles. Considerable edema of the papillae and corium developed with vascular and lymph vessel dilatation accompanied by an infiltration with various cells, of which eosinophils were prominent. Later parakeratosis and hyperkeratosis were present and in the corium granulation tissue developed. Bonnevie found that the histologic changes in upper layers of the epidermis resembled the reticular degenerative changes seen in variola except that the multilocular vesicles that were formed in milkers' nodules remain microscopic. The hyperkeratosis present probably prevented the vesicles from becoming larger or reaching the surface. The exudate in the epidermal vesicles of milkers' nodules



Fig. 1 (case 2).—Typical milkers' nodule with two secondary lesions. Photographed by Dr. R. H. Puumala.

however, in contrast to variola, does not become pustular, and the dermis of the nodules is characterized by the formation of granulation tissue.

REPORT OF CASES

CASE 1.—S. N., a white youth aged 16 years, had never been vaccinated for smallpox. He spent his summer vacation on a farm, where he milked cows that had "crusted sores" on their udders. A small dark red pea sized papule developed between the first and second fingers of the right hand. The lesion slowly grew larger until it became the size of a cherry. At the end of three weeks he consulted his local physician, who described the lesion as a semisolid brownish red nodule 1 cm. in diameter which was covered by a dried grayish epidermis, which he easily removed. The patient was referred to me and examination showed a nodule 0.75 cm. in diameter of red granulation tissue. One right axillary gland was enlarged to the size of a walnut and was slightly tender. My first diagnostic impression was pyogenic granuloma. However, the unusual history of contact with sores on cattle prompted the performance of a biopsy, after which the remainder of the nodule was cauterized. Healing was uneventful and took place

10. Stark, A. M.; Tiesenhause, M. M.; Gozanskaja, N. M.; Skrozky, E. W., and Schtshastny, D. S.: Ueber die Pockenetiologie der sogenannten Melkernoten, Arch. f. Dermat. u. Syph. 170: 38, 1934.

11. Gottron, Heinrich: Beitrag zur Aetiologie de Melkernoten, Dermat. Ztschr. 58: 207 (May) 1930.

12. Tappeiner, Sepp: Zur Frage der vakzinalen Aetiologie der Melkernoten, Wien. klin. Wchnschr. 51: 1061 (Sept. 23) 1938.

13. Lipschutz, B.: Paravaccine, in Jadassohn, Josef: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 2, p. 80.

14. Dolgov, A., and Morosov, M.: Zur Frage der Aetiologie der Melkernoten, Sovet. vestnik Dermat. 9: 338, 1931.

15. Zenin, A. S.: Beitrag zur Kenntnis der sogenannten "Melkernoten," Dermat. Wchnschr. 94: 605 (April 30) 1932.

16. Falchi, Giorgio: Rilevi clinici e ricerche sperimentali sui noduli vaccinali, Gior. ital. di dermat. e sif. 77: 181 (April) 1936.

17. Bonnevie, Paul: "Milkers' Warts": Infection from "False Cowpox" with Paravaccinal Virus, Brit. J. Dermat. 40: 164 (April) 1937.

18. Groth, A.: Zur Aetiologie der Melkernoten, München. med. Wchnschr. 76: 2128 (Dec. 20) 1929.

19. Kaiser, M., and Gherardini, Maria: Studien über Melkernoten, Arch. f. Dermat. u. Syph. 169: 77, 1935.

20. Woringe, F.: Deux nouveaux cas de tubercules du trayeur, Bull. Soc. franç. de dermat. et syph. (Réunion dermat.) 41: 197 (Feb.) 1934.

21. Unna (Die Histopathologie der Hautkrankheiten, Berlin, A. Hirschwald, 1894) described reticular degeneration as a vacuolar deterioration of the cells of the upper rete malpighii producing large clear cells in which some of the cellular membranes rupture, producing multilocular vesicles.

within ten days. The patient was vaccinated two weeks after the lesion healed; a positive reaction developed which produced a typical scar.

CASE 2.—J. H., a patient of Dr. R. H. Puumala of Cloquet, Minn., a white youth aged 18 years, was never vaccinated and had milked cows on his father's farm for the past nine years.

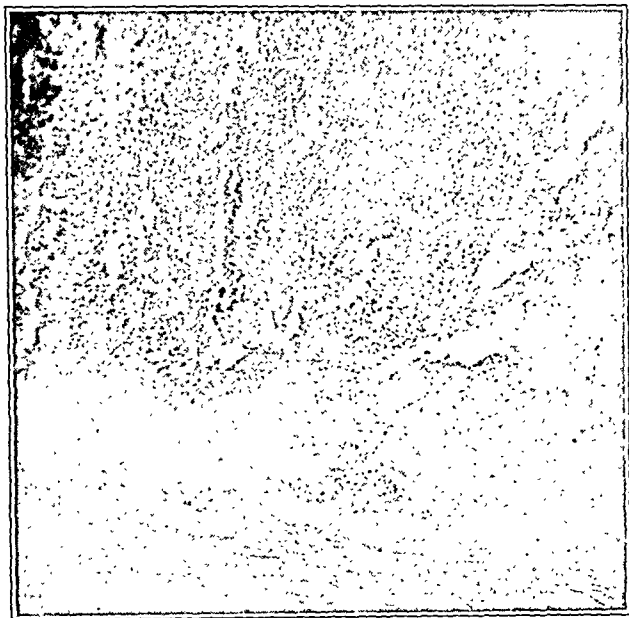


Fig. 2.—Low power magnification of section from case 2 showing hyperkeratosis, multilocular vesicles and dense cellular infiltrate in the dermis; stained with hematoxylin-eosin.

In June 1939 he first noticed that some of the cows developed crusts on their udders. About the middle of August a small papule developed at the site of a scratch on the medial surface of the first finger of the left hand; this lesion slowly grew larger and four days later two others started on the dorso-lateral aspect of the right wrist and thumb. My examination on August 28 showed a hard, nonpainful, brownish red nodule on the left index finger, 1 cm. in diameter and 4 mm. high. The top surface was slightly delled. The lesions on the right hand were pea sized papules with a small central vesicle. Both right and left epitrochlear glands were enlarged to about the size of a hazelnut and two axillary glands were the size of a walnut and slightly tender. A punch biopsy was taken of the first lesion on the left index finger. Half of the material was emulsified and some of it was instilled into the scarified cornea of two rabbits and the rest was injected into the skin and foot pads of two guinea pigs. The other half was placed in solution of formaldehyde, embedded in paraffin, sectioned and stained with hematoxylin and eosin. All lesions were dressed with sterile petrolatum and observed every other day by Dr. Puumala, who reported that the lesions were entirely healed in one month without any scar except at the site of the biopsy wound. At this time he vaccinated the patient with smallpox vaccine, which produced a positive reaction that resulted in the classic scar.

CASE 3.²²—Mrs. M. W., a white woman aged 27, seen Sept. 1, 1939, milked cows at irregular intervals during the past year and stated that one of the animals had sores about the udder. Three weeks previous to the time of consultation she noticed a lesion on the right thumb which continued to grow. Examination showed a round, bluish red button-like tumor 1.5 cm. in diameter on the first joint of the right thumb. The center was slightly depressed and whitish. There were no palpable enlarged lymph nodes. The nodule was removed and divided in half; one portion was fixed in solution of

formaldehyde and sectioned and stained with hematoxylin and eosin. The other part was emulsified and some of it instilled in the scarified cornea of a rabbit and the rest injected into the thigh and skin of two guinea pigs.

CASE 4.—Mrs. L. W., a farmer's wife aged 28, observed Sept. 29, 1939, stated that she developed about three weeks previously an eruption on the right little finger. Examination revealed an elevated bluish red semisolid tumor 1 cm. in diameter on the right little finger. The top surface of the growth was easily removed, leaving a red granulating surface. A biopsy was taken and the lesion cauterized, after which uneventful healing took place.

EXPERIMENTAL RESULTS

The corneas of all rabbits inoculated with material in cases 2 and 3 were watched daily for a period of two weeks and no reaction took place and the corneas remained clear. The guinea pigs were kept under observation for two months. No inflammatory reaction occurred at the injection sites. They were killed at this time and no evidence of any infection could be found at pathologic examination. Cultures were made on all types of routine mediums with the emulsified material from cases 2 and 3 and no growth was obtained.

HISTOLOGY

The microscopic examinations in my four cases were similar to those described in the literature and the essential features which I found may be summarized as follows:

There was considerable increase in the stratum corneum with hyperkeratosis and parakeratosis (fig. 2). Acanthosis and spongiosis were present and in the upper layers of the rete malpighii there was an increased intracellular edema which produced in some scattered

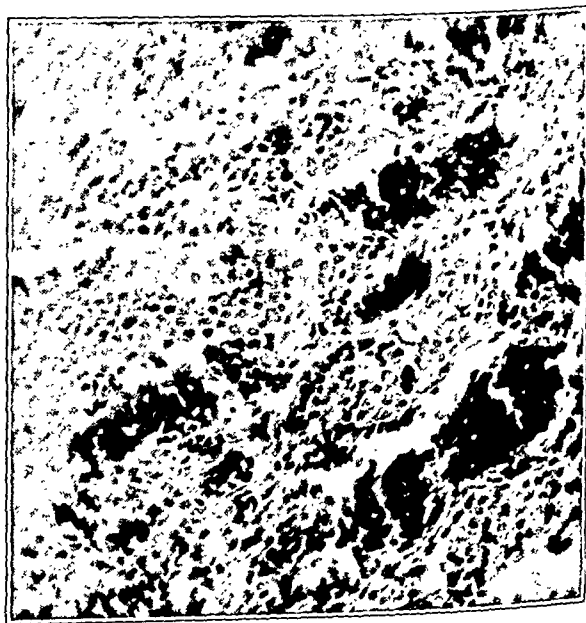


Fig. 3.—High power reproduction of figure 2, showing the dermis with dense multicellular infiltrate and marked blood vessel dilatation.

areas enlarged clear cells with only a thin cellular membrane and in other areas there were microscopic multilocular vesicles. The dermis was edematous with an increased vascularity (fig. 3) and dense cellular infiltration was present which disrupted the epidermal-dermal junction. This infiltrate was made up principally of

²² Cases 3 and 4 were observed by Dr. Stephen Epstein of Marshfield, Wis., and are recorded with his permission. The biopsy material was studied by me.

lymphocytes and also many plasma cells, eosinophils and an occasional giant cell and polymorphonuclear leukocyte. The increased intracellular edema with the formation of microscopic multilocular vesicles could be interpreted as a mild degree of reticular degeneration as described by Unna. In none of the microscopic sections studied was there any evidence of pustulation.

COMMENT

It is quite evident both clinically and histologically that the lesions occurring in the four cases described are similar in nature to those recorded in the German literature as "melkerknoten." All individuals afflicted had been engaged in milking cows on whose udders open ulcers or crusted lesions had been present. The cause of milkers' nodules is undoubtedly infectious, because the condition is self limited, healing spontaneously without treatment and apparently leaving an immunity to further similar inoculations. My inability to demonstrate any bacteria both by culture and by animal inoculation, plus the fact that many investigators have found inclusion bodies in a microscopic section, would indicate that the infecting agent is a filtrable virus.

The relation of this virus to vaccinia is still in a controversial state. The first to show any definite relation between the two were Schultze, Seifried and Schaaf. Paschen and Groth, however, believed that these cases were vaccinia and not true milkers' nodules. Experimental work of Stark and his co-workers supported the theory that the organism of milkers' nodules was of decreased virulence because only after repeated transfers to the same species of animals were they able to show conclusive evidence that the virus had the characteristics of variola vaccine.

It is generally agreed that for a virus to be similar to that of variola a positive Paul test must be obtained and the individual infected should acquire an immunity against vaccine virus. The majority of investigators of milkers' nodules have been unable to obtain positive Paul reactions from their cases and most of their patients have not acquired any immunity to smallpox vaccine. My results of a negative Paul test in two of the cases and a lack of immunity to vaccination as demonstrated in two others agrees with most authors. Therefore, because of these two facts along with the difference in the histologic picture and in the clinical course of milkers' nodules there does not seem to be much evidence to support any relation to variola vaccine. On the other hand, the pathologic process of milkers' nodules seems to show a close similarity to paravaccinia, as neither of the disorders produces immunity to subsequent inoculation with vaccine virus, the Paul test is negative and the microscopic appearances are similar in the two instances.

SUMMARY

1. Four cases of milkers' nodules, which is an infection of human beings acquired by milking diseased cows, were observed.
2. No relation between milkers' nodules and vaccinia could be demonstrated in these cases, as the Paul test, which was performed with material from two cases, was negative and two of the infected persons showed no immunity to smallpox vaccination.
3. The clinical course of milkers' nodules and the distinct variations in the pathologic picture are further evidences that this disease shows no relation to variola vaccine.

4. The cause of milkers' nodules is apparently a virus, which may be either an attenuated or biologic modification of vaccine virus. From all evidence it more closely resembles the paravaccine of Lipschutz.

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ABSTRACT OF DISCUSSION

DR. M. E. OBERMAYER, Chicago: Dr. Becker's presentation is thorough and complete, and it answers a long-felt need. In the United States, large sections of which are agricultural, an occupational disease among milkers is bound to be far more widespread than is indicated by the scarcity of case reports. There is still a great deal of controversy concerning the etiologic agents of the disorder. The only point on which the various investigators agree is that the condition is undoubtedly caused by a filtrable virus. In regard to the nature of the virus there are three schools of thought: (1) that the virus of milkers' nodules is identical with that of vaccinia, (2) that the virus of milkers' nodules represents an attenuated or biologically modified vaccinia virus or (3) that the virus of milkers' nodules has nothing to do with that of vaccinia but is identical with the virus of paravaccinia of Lipschutz. From what Dr. Becker said and from some additional references it seems that the evidence gathered for each of the three points of view is sufficiently strong to substantiate the choice of virus assumed to be responsible in each particular case which was studied. If to prove the identity of the virus of milkers' nodules with that of vaccinia three criteria must be met, namely (a) a positive Paul test, (b) demonstration of Guarnieri bodies and (c) failure to produce a positive take in the patient by ordinary antimallpox vaccination, satisfactory proof has been obtained though only in a small number of instances. The second assumption, that the virus represents an attenuated or biologically modified vaccinia virus, has been substantiated by the properties which the virus has exhibited after repeated animal transfers. The results of Dr. Becker's study led him to conclude that the third theory about the etiologic agent, supported by the evidence from his own cases, is the most acceptable. When reviewing the experimental data critically, I feel that the evidence which has been presented in favor of each of the three suggestions need not necessarily be considered conflicting if it is assumed that milkers' nodules represent a clinical entity caused by filtrable viruses of different kinds. The disorder may be caused at times by the ordinary virus of vaccinia, more often by an attenuated or biologically altered vaccinia virus and frequently by the virus of paravaccinia. The fact that the viruses of vaccinia and of paravaccinia have been found simultaneously in the same lymph is suggestive. Moreover, there seems to be evidence that the clinical aspects of the disease on the udders of the animals are not uniform. Thus the assumption of multiple etiologic agents of the disorder seems to me a logical means of bringing the seemingly conflicting evidence into agreement.

DR. C. GUY LANE, Boston: This condition is relatively unusual. The photograph which was shown on the screen was made last fall of these two lesions of three weeks' duration. The lesions presented themselves within two or three days after this man started working on a farm milking cows. He had not done this work for some twenty years previously. He noticed small erosions first, at the sites of friction between his fore and middle fingers following the beginning of his new job of milking. Then there was gradual development at the sites of the lesions which were shown on the screen. There were vesicles at the start, blisters that became eroded and then gradually became elevated. In one axilla there were one or two palpable tender glands. Our cultures at the hospital showed only staphylococci. The interpretation of the biopsy was at that time simply chronic inflammatory reaction. There is nothing known in this particular case with reference to the condition of the cow. The lesion subsided relatively readily under mild antiseptic therapy. It is interesting to review these cases and analyze our reasons for deciding that these are occupational. In the first place they occur so far as we know only in the agricultural occupations, those having to do with animals. The lesions are consistent with those which have previously been described in the literature

The time relationship is correct since this condition appears relatively few days after the patient has begun the job. Again, their site of onset is the site of the maximum trauma, or the site of the particular trauma, where greatest friction occurs, and as far as is known at present there is no other known source of this infection.

DR. FREDERIC T. BECKER, Duluth, Minn.: From the contact I have had in the Scientific Exhibit, I am sure that milkers' nodules are not rare in this country. Many doctors who are located in dairying communities have seen these cases at intervals. I think that calling attention to it will bring forth many new cases.

TROPHIC LESIONS IN THE DISTRIBUTION OF THE TRIGEMINAL NERVE

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To the neurologist, bona fide trophic changes are lesions appearing in tissues which have been deprived of certain qualities of sensation, particularly those of pain and temperature.

That portion of the face which is supplied by the trigeminal nerve may be thus denervated by a number of organic disturbances. The neurosurgeon accomplishes this by sectioning the nerve through its peripheral branches, the gasserian ganglion, the posterior root or, more selectively, by the newest procedure devised by Sjöqvist,¹ namely cutting the descending spinal tract in the medulla.

Occasionally a tumor or an inflammatory process may be so peculiarly situated near the ganglion or in the brain stem as to interrupt the sensory function and cause some degree of anesthesia in the face. Most striking is the analgesia produced by two well known lesions of the medulla, namely occlusion of the posterior inferior cerebellar artery and syringobulbia.

The whole subject of trigeminal nerve function has undergone a recent renaissance and a wealth of literature has emerged, representative of which are the studies of Sjöqvist;¹ Walker;² Rowbotham;³ Smyth⁴ and Lewy, Groff and Grant.⁵ In all these discourses little is said of neurotrophic lesions in the trigeminal area for the reason that such disturbances are rather rare. This, of course, is true only if one excludes the simple herpetic eruptions about the lips which occur in many febrile diseases and if one also makes an exception of the corneal complications following section of the trigeminal nerve. The more malignant herpes which is associated with persistent neuralgia is of uncommon occurrence. Peet⁶ found only three cases among 400

sufferers with facial neuralgia and quoted Frazier as having encountered but one instance in 520 cases, while Cushing mentioned herpetic neuralgia in only three of 332 operations on the gasserian ganglion.

This discussion concerns itself with trophic lesions which are nonherpetic in nature. The three examples which are presented have all been studied by competent dermatologists, who found no explanation for the appearance of the lesions except on a neurotrophic basis. These cutaneous phenomena have these features in common: They are implanted on areas definitely devoid of pain and temperature sense and they all conform sharply to neuroanatomic delineations. They differ in that the interruption of sensation occurs at different levels in the trigeminal system: In the first case the changes in the skin followed a gasserian section, in the second case it is clinically assumed that the disturbance was caused by an occlusion of the posterior inferior cerebellar artery, and in the third case the symptoms were typical of syringobulbia.

DERMATITIS FOLLOWING GASSERIAN SECTION

Simple erythematous eruptions following trigeminal nerve section are unusual, unpredictable and puzzling phenomena. In a review of 107 cases in which the ganglion or the posterior root was cut, Becker⁷ was able to find only five cases in which cutaneous manifestations were presented. He himself reported the case of a 47 year old woman who developed an erythematovesicular eruption, which appeared three weeks after an operation for trigeminal neuralgia.

The following case, of a cutaneous disturbance previously reported by Netherton⁸ from the point of view of a dermatologist, is now reviewed after further study of the process and its relation to the neural defect:

CASE 1.—A woman aged 44 came to the Cleveland Clinic in March 1930 for relief from paroxysmal facial neuralgia, characterized by a hot, jagging pain over the left side of about five years' duration. The attacks were induced by rubbing the upper or lower eyelid and by talking or chewing.

Nothing of significance was elicited from her history except that she had occasional attacks of urticaria and a mild eczema had developed in the flexor regions of the extremities.

Surgical treatment consisted of a total section of the first and second divisions and a partial section of the third division of the trigeminal nerve. A year later an erythematous plaque developed on the left side of the forehead, to be quickly followed by similar lesions over the left temple, the lower lip, the left cheek and the left side of the nose. The areas gradually became confluent, and a sharp line of demarcation between normal and abnormal skin developed in the middle of the face. The erythematous flush was particularly prominent in the areas supplied by the first and second divisions of the severed trigeminal nerve and faded diffusely into the zone of the third division.

Neurologic examination disclosed marked hypesthesia to all qualities of sensation in the areas supplied by the ophthalmic and mandibular divisions and total anesthesia in the area assigned to the second division. There was typical absence of the corneal reflex on the affected side, but no evidence of involvement of the sympathetic nerves. Thermocouple readings were similar on the two sides of the face.

The cutaneous disturbance remained strictly unilateral in distribution. It was not accompanied by pain or other subjective disturbances. There was no induration of the underlying tissues. Exposure to cold, heat, wind, soap and water produced periodic exacerbations of an exudative inflammation, followed by increased desquamation.

7. Becker, S. W.: Dermatitis in Association with Disease or Injury of the Peripheral Nerves, *Arch. Dermat. & Syph.* 12: 235-241 (Aug.) 1925.

8. Netherton, E. W.: Persistent Dermatitis: Unusual Sequela of Radical Operation for Trigeminal Neuralgia, *J. A. M. A.* 100: 722-724 (March 11) 1933.

Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

From the Division of Neuropsychiatry, Cleveland City Hospital, and the Department of Nervous and Mental Diseases, Western Reserve University School of Medicine (Dr. Karnosh).

1. Sjöqvist, O.: Studies on Pain Conduction in the Trigeminal Nerve, *Acta psychiat. et neurol. (supp.)* 17: 1-139, 1938.

2. Walker, A. Earl: Anatomy, Physiology and Surgical Considerations of the Spinal Tract of the Trigeminal Nerve, *J. Neurophysiol.* 2: 234-248 (May) 1939.

3. Rowbotham, G. F.: Observations on the Effects of Trigeminal Denervation, *Brain* 62: 364-380 (Dec.) 1939.

4. Smyth, G. E.: The Systemization and Central Connections of the Spinal Tract and Nucleus of the Trigeminal Nerve: A Clinical and Pathological Study, *Brain* 62: 41-87 (March) 1939.

5. Lewy, F. H.; Groff, R. A., and Grant, F. C.: Autonomic Innervation of the Eyelids and the Marcus Gunn Phenomenon, *Arch. Neurol. & Psychiat.* 37: 1289-1297 (June) 1937.

6. Peet, M. M.: Postherpetic Trigeminal Neuralgia: Persistence of Pain After Section of the Sensory Root of the Gasserian Ganglion, *J. A. M. A.* 92: 1503-1505 (May 4) 1929.

All this embarrassed the patient greatly and handicapped her in business. She managed a meat stall in a large open market. Would-be customers glanced at her facial blemish and passed on to trade with her competitors. Despite various topical applications, the condition remains essentially unimproved at the present time. Biopsy of the skin was not allowed.

In attempting to explain the relation of eczema to nerve injury such as is here presented, dermatologists can offer only an empiric opinion. Bruck⁹ expressed the belief that many skin eruptions of this nature may be of true neural origin, but only when the damage is limited to the somatic sensory fibers while the sympathetic and vasomotor mechanisms are intact. Such an explanation, however, is inadequate, for this very situation obtains in almost every case of neuralgia following trigeminal nerve section and yet eczema rarely follows. The preexisting allergy may be significant, and the singular disposition to eczema in other parts of the body must be considered as a factor in determining this unusual reaction to facial hemianesthesia.

TROPHIC CHANGES FOLLOWING THROMBOSIS OF THE POSTERIOR INFERIOR CEREBELLAR ARTERY

Bruck's theory is even less tenable in explaining trophic changes which occur on the face after an occlusion of the posterior inferior cerebellar artery, for not only is there marked analgesia of the homolateral

CASE 2.—A white man aged 48, a glazier, was suffering with diabetes, which was well controlled by 5 units of insulin before each meal. On the morning of Nov. 9, 1934, he was awakened by a peculiar sensation of numbness over the entire left side of the face and a deep, gnawing, burning pain about the left eye. On rubbing his face he found the right side to be moist with perspiration and the left side utterly dry. On

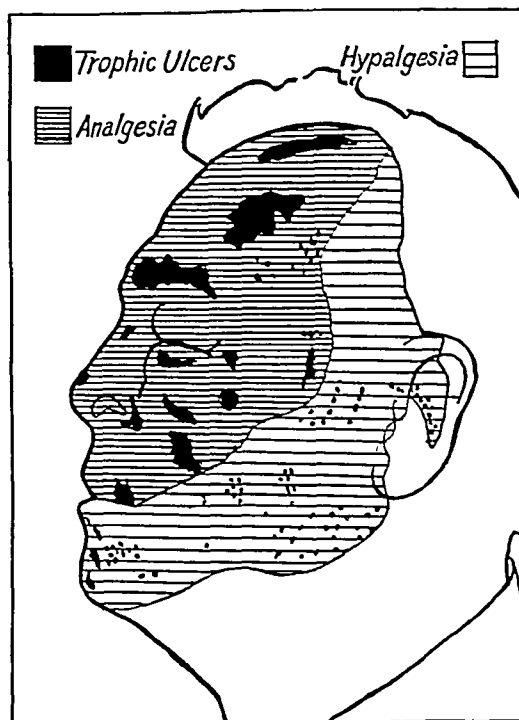


Fig. 2 (case 2).—Distribution of trophic lesions and of analgesia due to vascular softening of the lateral portion of the medulla following an occlusion of the posterior inferior cerebellar artery. Both ulceration and analgesia conform to the peripheral orientation of the trigeminal nerve. The area supplied by the geniculate portion of the facial nerve is spared.



Fig. 1 (case 2).—Appearance of lesions.

side of the face but the sympathetic and vasomotor fibers are frequently involved in the same destructive process. Irrespective of the damage to the vegetative nerve components, the cutaneous changes may become extensive and pernicious and may cause severe distortion of the tissues of the face.

attaining the sitting position in bed he became very dizzy and on attempting to stand he swayed strongly to the left.

The neurologic components of significance were as follows: The pupils were unequal, the left being very small and reacting slightly to the flashlight. There was a clockwise rotatory nystagmus when the gaze was directed to the left. The left corneal reflex was absent. The greater portion of the left trigeminal area was analgesic, while tactile sense was only moderately impaired. The sensory defect was pronounced in those areas in which the patient experienced the deep pain; that is, at the root of the nose and just under the left eye. The left side of the palate was poorly elevated. Excursion of the vocal cords was symmetrical. The left abdominal and cremasteric reflexes were absent. In the Romberg test the patient swayed violently to the left side.

The ulcers appeared about six weeks after the onset of the illness as small red patches at the left angle of the mouth, under the left eye and on the left side of the nose. These were entirely painless and gradually spread, leaving in their wake a reddened, puffy, indurated, crusted skin, which broke down again and again until there was considerable deformity of the face. Lesions appeared in the scalp, anterior to the ear and on the chin but never outside the left trigeminal area. Biopsy of the skin demonstrated no specific disease.

These distressing cutaneous changes on the left side of the face were accompanied by a Horner syndrome. There was a marked difference in the temperature of the skin on the two sides of the face. The Minor starch and iodine test, according to the technic outlined by List and Peet,¹⁰ demonstrated com-

9. Bruck, C.: Nervenschädigung und Eksem: Ein klinischer Beitrag zur Frage der Eksempathogenese. *Dermat. Ztschr.* 55:7-13 (Dec.) 1929.

10. List, C. F., and Peet, M. M.: Sweat Secretion in Man: I. Sweat Responses in Normal Persons. *Arch. Neurol. & Psychiat.* 30:1228-1237 (June) 1938.

plete paralysis of sweating on the left side. A resection of the inferior cervical ganglion was done with the hope that by further increasing the blood supply the cutaneous lesions would improve. The procedure merely served to increase the enophthalmos. To roentgen therapy the response was equally indifferent.

At the present time the trophic process has advanced into the eyeball, the cornea being cloudy and showing extensive vascularization in its lower segments. The conjunctiva and all periorbital tissues are markedly edematous.

The trophic disease in this case appears to be in direct proportion to the degree of analgesia, the most severe lesions being found in the first and second divisions of the trigeminal area (figs. 1 and 2). The skin supplied by the mandibular division is only moderately analgesic, and the trophic changes are minimal. The nature and distribution of the skin eruptions are

objective testimony that the descending spinal tract of the trigeminal nerve is fundamentally arranged to conform to the peripheral distribution of the nerve, a finding about which there is general agreement.

TROPHIC LESIONS IN SYRINGOBULBIA

No concerted opinion exists, however, with respect to the significance of the sensory changes which may occur in syringobulbia. Such tangible evidence of sensory loss as trophic ulceration of the face is usually wanting in this medullary disease. It is true that hyperostosis of the facial bones has been noted in syringobulbia, and in 1930 Thomas¹³ described a case in which there was thickening of the left side of the face, but trophic changes in the skin itself are not mentioned in any clinical reports on this disease.

CASE 3.—A stocky white woman aged 37 first noticed numbness of the left hand and shoulder and the left side of the face five years before she came to the attention of the neurologic clinic at the City Hospital. The numbness of the face was more irritating than painful. She applied a heat lamp to the area, and quickly there developed shallow, painless ulcers about the left ear. These extended directly upward into the scalp and downward along the angle of the jaw.

The positive observations in the neurologic examination were as follows: The left corneal reflex was absent and there was a rotating type of nystagmus, more pronounced when the gaze was directed to the left. The gag reflex was absent on the left side, and the left vocal cord was inactive during phonation. The posture was stooped, with a thoracic kyphosis. There was slight atrophy of the muscles of both shoulder girdles, more marked on the right side. In the left hand the thenar eminence was small; in the right hand there was considerable atrophy of the interosseous tissues.

The sensory examination revealed anesthesia to pain and temperature on the left side of the head, limited anteriorly by a line passing from the vertex downward over the malar prominence to the angle of the jaw. This area of total analgesia extended backward into the scalp and downward over the neck and in mantle-like fashion over both shoulders to the elbows and the nipple levels of the chest. In the face, anterior to the analgesic zone, was a narrow band of hypalgesia, while the area about the nose, mouth and eye was essentially normal in pain and temperature sense. Tactile sense was well preserved everywhere, demonstrating the familiar dissociation of sense characteristic of syringomyelia. There was no involvement of the sympathetic nervous system.

The facial lesions appeared in the area which is supplied by overlapping branches of the trigeminal and the highest cervical nerves. The erosions spread, healed occasionally with a thick epithelial covering, only to reopen and increase in size. They eventually extended deep into the external auditory meatus. After many sporadic attempts at healing, a progressive induration ensued, leading to considerable cicatrization, particularly below the ear.

In this case the disposition of ulcers furnishes objective evidence of the peculiar nature of the sensory disturbances which occur in the trigeminal area in syringobulbia. Both the trophic ulceration and the sensory changes utterly ignore the peripheral orientation of the fifth nerve and dispose themselves in a segmental or concentric fashion converging on the nose and mouth (figs. 3 and 4). The erosions are equally heedless of the sensory architecture about the ear, involving the geniculate or facial components about the external auditory meatus and showing no regard for the peripheral topography of the auricular and occipital branches of the cervical plexus.

The concentric sensory zoning on the face is not an uncommon occurrence in syringobulbia and is observed



Fig. 3 (case 3).—Trophic ulcers and sensory defect in a case of syringobulbia.

in harmony with most of the descriptions of sensory change in the Wallenberg syndrome. Moreover, an identical sensory disturbance was found by Sjöqvist¹ and Walker² and by Grant, Groff and Lewy¹¹ in patients after tractotomy, so that one is fairly certain that this patient had a lesion in the descending spinal tract. Not only do the lesions orient themselves in their intensity according to the three peripheral divisions of the fifth nerve but both ulcerations and analgesia avoid the area assigned by Ramsay Hunt¹² to the sensory portion of the facial nerve. Whatever the pathologic process may be, this trophic change in a disease of the lateral portion of the medulla offers

11. Grant, F. C.; Groff, R. A., and Lewy, F. H.: Section of the Descending Spinal Root of the Fifth Cranial Nerve, *Arch. Neurol. & Psychiat.* 43: 498-509 (March) 1940.

12. Hunt, Ramsay: Geniculate Neuralgia (Neuralgia of the Nervus Facialis): A Further Contribution to the Sensory System of the Facial Nerve and Its Neurologic Conditions, *Arch. Neurol. & Psychiat.* 37: 253-285 (Feb.) 1937.

13. Thomas, André: Forme unilatérale et sensitive de la syringomyélobulbie; coexistence d'apophyses cortiformes de la 7 cervicale, *Presse méd.* 38: 611-612 (May) 1930.

in no other disease. Schlesinger¹⁴ in 1895 and von Sölder¹⁵ in 1899 noted that loss of pain sense first appeared in the scalp and advanced toward the nose and mouth. Dejerine¹⁶ made the same observation and came to the conclusion that the trigeminal structures in the brain stem are segmentally arranged in terms of concentric circles converging on the nose. Woods¹⁷ supported the same hypothesis after reporting two cases of syringobulbia. We investigated three cases of this disease and in only one was this type of sensory disturbance absent. Yet Taylor, Greenfield and Martin¹⁸ and Jonesco-Sisesti¹⁹ did not agree that this segmentation of pain sense is typical of syringobulbia. After making excellent clinicopathologic correlations, Smyth⁴ ridiculed this concept of concentric zoning, although he conceded that it may be occasionally encountered. For this he had no explanation. Perhaps, as Sjöqvist suggested, this sensory disturbance is peculiar to syringo-

clearly known, and his proof that it is not segmentally arranged is not very convincing.

In the case presented here the trophic erosions of the skin are so disposed as to support the theory that this tract conveying pain and temperature sensations across the medulla retains its primitive lamellar or segmental arrangement in the same manner as does its homologue in the spinal cord, namely the spinothalamic tract. That the latter structure, which is equally susceptible to syringomyelia, possesses this anatomic feature has been demonstrated in the clinical investigations of Tilney and Elsberg²⁰ and by the neurosurgical studies of Hyndman and Van Epps.²¹

SUMMARY

Neurotrophic changes in the trigeminal area of a nonherpetic type may occur in any disease which destroys the fibers conveying pain and temperature sense. That they are uncommon is probably due to the fact that the face is instinctively better protected from trauma than are other parts of the body which become analgesic. The erosive process on the skin can exist independent of sympathetic involvement. Skin eruptions of a trophic nature may arise as unpredictable and embarrassing sequelae of nerve section for facial neuralgia.

Destructive lesions of the brain stem produce trophic disorders the distribution of which offers additional data as to the manner in which the fibers of the trigeminal pathways are arranged within the central nervous system. Vascular softenings which usually involve the lateral portions of the medulla produce sensory changes which conform to the peripheral distribution of the trigeminal nerve, while a process which primarily destroys the inner structures of the brain stem leads to analgesic areas with a concentric zoning converging on the nose and mouth.

ABSTRACT OF DISCUSSION

DR. MAX MINOR PEET, Ann Arbor, Mich.: I have no explanation for these trophic disturbances or diseases involving the trigeminal tract. I have seen three cases of apparent trophic disturbance in about 1,000 operations for section of the sensory root of the gasserian ganglion. Three tenths of 1 per cent is a very small incidence. In two of those cases there were rather marked paresthesias. This is a peculiar sensory disturbance when the face itself is absolutely anesthetic. The patient feels crawling or burning sensations and itching or tickling and more or less constantly traumatizes his face. One of these patients—and they all were elderly—constantly rubbed the nose or picked it, and I think possibly that was the cause of the disturbance. Both of these elderly persons who had this type of lesion had a slow, almost benign, ulceration starting in the ala of the nose, and it finally went to complete destruction of the lower corner of the ala and then extended slowly, gradually, over a number of years, out to the adjacent part of the cheek. The ulceration was exceedingly superficial. It would be healed much of the time and then break out again apparently under direct trauma. The patients both said they had these paresthesias, that they couldn't help picking at the nose or face, and they both thought this constant trauma was a factor. The third case developed in the ophthalmic division in the forehead. The patient came back several years after operation with typical whitish scars in the forehead, such as are seen after a true herpes, and I am not certain whether this patient actually developed a true herpetic lesion superimposed on an anesthetic area following section of the sensory root. In the last patient that had this destruc-

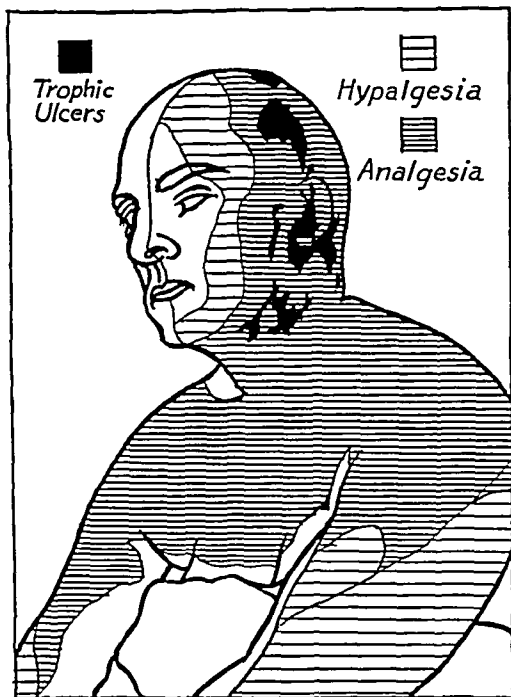


Fig. 4 (case 3).—Peripheral nerve topography is ignored, and the lesions of the skin as well as the analgesic areas are arranged in a concentric manner, with the zones converging on the nose and mouth.

bulbia because the disease primarily involves the second sensory neuron of the trigeminal nerve, the so-called quintothalamic tract. In its orderly ascent through the reticular portion of the brain stem the pathologic process exposed the segmental structure of this tract and its nucleus. It is conceivable that the irregular sensory disturbances observed by some writers are produced by a process which destroys parts of both the first and the second sensory neuron. Smyth admitted that the anatomic position of the quintothalamic tract is not

14. Schlesinger, H.: *Die Syringomyelie*, Leipzig, Franz Deuticke, 1895.

15. von Sölder, F.: *Der segmentale Begrenzungstypus bei Hautanästhesien am Kopfe, insbesondere in Fällen von Syringomyelie*, *Jahrb. f. Psychiat. u. Neurol.* 18: 458-478, 1899.

16. Dejerine, J.: *Sémiologie des affections du système nerveux*, Paris, Masson & Cie, 1914, p. 800.

17. Woods, A. H.: *Segmental Distribution of Spinal Root Nucleus of the Trigeminal Nerve*, *J. Nerv. & Ment. Dis.* 110: 91, 1913.

18. Taylor, J.; Greenfield, J. G., and Martin, J. P.: *Syringomyelia and Syringobulbia*, *Brain* 45: 323-356 (Dec.) 1922.

19. Jonesco-Sisesti, N.: *La syringobulbie: Contribution à la physiopathologie du tronc cérébral*, Paris, Masson & Cie, 1932.

20. Tilney, Frederick, and Elsberg, C. A.: *Sensory Disturbances in Tumors of the Cervical Spinal Cord*, *Arch. Neurol. & Psychiat.* 15: 444-454 (April) 1926.

21. Hyndman, O. R., and Van Epps, Clarence: *Possibility of Differential Section of the Spinothalamic Tract*, *Arch. Surg.* 38: 1036-1053 (June) 1939.

tion of the ala of the nose I had our dermatology department study the patient. There were no signs of malignancy. There were semicutaneous changes in other parts of the face and body and the dermatology department didn't want to say whether this was trophic, whether this was actually in any way related to section of the sensory root of the gasserian ganglion or whether it was a traumatic lesion incident to the paresthesia that the patient was suffering. It seems that, if we are going to assume that these are trophic, they ought to occur in a much higher percentage of cases. We know the very high incidence of herpes which occurs after operation. For a long time I assumed that these herpetic manifestations were due to injury directly to the gasserian ganglion incident to its exposure. I do not take up the ganglion, of course, but strip the dura from it. Then on one patient I sectioned the sensory root by the posterior approach. I was nowhere near the ganglion, I could not have disturbed it, and that individual had the most extensive herpetic lesions on the lower half of the face of any patient I have ever seen. So it is not due to direct trauma to the gasserian ganglion.

DR. A. EARL WALKER, Chicago: In view of the fact that the denervated areas are commonly said to be particularly susceptible to infection and injury, it is remarkable that following retrogasserian neurectomy so few cases such as have been described today are reported. From France in 1936 Dechaume and Delibéros (*Rev. de stomatol.* 38:194 [March] 1936) reported an ulcerative lesion of the maxillary mucous membrane of a patient who, twelve years before, had a retrogasserian neurectomy. They stated that such a complication was unique in their experience. In their case trauma was probably a precipitating factor, as Dr. Peet has emphasized, for the patient had worn an ill fitting denture which bothered her a great deal. I am more interested in the type of sensory disturbance which the authors have discussed. It has been shown that section of the descending root of the trigeminal nerve, in the manner Sjöqvist devised, produces sensory changes, a marked analgesia with relative hypesthesia in the divisional portions of the face; that is, it involves the first, second or third division but does not give rise to the onion skin type of sensory disturbance which is seen occasionally in syringobulbia. Neuro-anatomy does not tell the reason for this difference, although it has now been shown that there is a definite laminar arrangement of the tracts derived from both the nucleus of the descending portion of the trigeminal nerve and the main trigeminal nucleus. The onion skin type of sensory disturbance is analogous to the stocking or glove type of sensory disturbances in the arms or legs. We know that such sensory disturbances do not usually occur with spinal cord lesions, but they are seen with lesions of the thalamus and cerebral cortex. This suggests that there is a rearrangement of the nerve fibers in their passage from the spinal cord to the thalamus and to the cortex. It is quite probable that such a rearrangement of the fibers occurs very shortly after their origin in the spinal cord or from the descending root in the fifth nerve. Hence, as Sjöqvist, Smyth, Stratford and others have suggested, syringobulbia involving the secondary trigeminal pathways would give rise to the type of sensory disturbance which is more commonly seen with lesions of the thalamus or cerebral cortex than the type of impairment which is seen with section of the primary sensory nerve fiber.

DR. BYRON STOOKEY, New York: I should like to confirm what Dr. Peet said. In a large series of trigeminal operations I have not encountered the type of lesions presented to us this morning. The only trophic disturbances, if they are trophic disturbances, that I have seen have been the ones Dr. Peet has described following the operation immediately, and then there has been another group of which I should think there are about seven or eight cases of so-called seborrheic dermatitis, a scaly, greasy condition found over the distribution of the fifth nerve, mostly in the first division, to a less extent in the second division, in those instances in which we have done a total section. With these two exceptions I have not encountered the type of lesion which has been presented. I am extremely interested in the presentation. I question whether we can call it trophic disturbances and I wondered, in view of the extreme rarity of the lesions following dorsal section, if they are necessarily alone to be attributed to the cutting of the fifth nerve root.

MELANOMA OF THE CENTRAL NERVOUS SYSTEM

REPORT OF THIRTY-FOUR CASES, IN NINETEEN OF WHICH THE DIAGNOSIS WAS VERIFIED BY OPERATION OR NECROPSY

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During the five weeks from April 1 to May 5, 1939, inclusive, we had occasion to make a diagnosis of melanoma of the central nervous system in four cases. The rapid succession of these four tragic experiences prompted us to carry out the present study.

A survey of the literature on melanoma reveals an almost endless list of contributions covering various phases of the subject. In this presentation we are not concerned with the histologic structure of melanoma but wish to stress the importance of melanoma from the neurologic standpoint. We are employing the terms "melanoma," "melanocarcinoma," "melanosarcoma" and "melano-epithelioma" synonymously.

That melanomas are a serious menace to life needs no comment. The frequency of their occurrence remains somewhat uncertain. Adair¹ reported that 400 cases were observed at the Memorial Hospital in Chicago during an eighteen year period. In 41,984 surgical specimens examined by the department of pathology at the Toronto General Hospital from January 1928 to January 1935 Plewes² found ninety-three melanomas, or an incidence of 0.2 per cent. Affleck,³ in a follow-up study of 170 patients who had melanomas, found that 115 died in less than three years and that 10 per cent were alive after a lapse of five years. Broders and MacCarty⁴ in their review said that the mortality rate was 86.8 per cent although they said that all their patients had not been heard from.

Two contributions on melanomas of the nervous system, one by the Wortises⁵ in 1936 and the other by Courville and Schillinger⁶ in 1939, leave little to be added to the general consideration of the subject. It may be well, however, again to call attention to the frequency with which melanomas involve the central nervous system and to urge rigid prophylaxis against this disease. As Adair has stated, "there is no tumor which places the clinician in such a mental state of helplessness as the melanoma once it has left the original site." The frequency with which melanomas metastasize to the central nervous system varies from 10 to 50 per cent according to different authors. In a series of 20,000 necropsies Courville and Schillinger noted twenty instances of melanoma; in eighteen of the cases there

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1. Adair, F. E.: Treatment of Melanoma: Report of Four Hundred Cases, *Surg., Gynec. & Obst.* 62: 406-409 (Feb. 15) 1936.

2. Plewes, F. B.: Malignant Melanomatosis, *Am. J. Cancer* 26: 732-737 (April) 1936.

3. Affleck, D. H.: Melanomas, *Am. J. Cancer* 27: 120-138 (May) 1936.

4. Broders, A. C., and MacCarty, W. C.: Melanoma-Epithelioma: A Report of Seventy Cases, *Surg., Gynec. & Obst.* 23: 28-32 (July) 1916.

5. Wortis, Herman, and Wortis, S. B.: Metastatic Melanoma Involving the Central Nervous System, *Arch. Neurol. & Psychiat.* 36: 601-611 (Sept.) 1936.

6. Courville, C. B., and Schillinger, R. J.: Metastatic Melanoblastomas of the Brain: Review of the Literature and Survey of Eighteen Cases, *Bull. Los Angeles Neurol. Soc.* 4: 8-22 (March) 1939.

was widespread metastasis. In nine, or 50 per cent, of the eighteen cases, the brain was involved. Bailey⁷ suggested a similar figure for involvement of the brain in the presence of generalized metastasis. He stated, however, that this figure may be somewhat high. In 1932 Dunlap,⁸ in a report of ninety-five metastatic tumors of the brain observed at the Mayo Clinic, said that he found only two melanomas. As a result of our present study this figure should be increased by several cases. In a series of 107 cases of metastatic tumor of the brain, Courville and Schillinger observed that the incidence of melanomas was 13 per cent.

MATERIAL

In the ten year period from 1930 to 1939 inclusive we have seen approximately 500 cases of melanoma. This number represents about 2 per cent of the total number of cases of malignant lesions seen during that period. Unfortunately a complete follow-up study in the 500 cases has not been possible; therefore accurate deductions cannot be made. In approximately a fourth of the cases of melanoma the primary tumor was situated in or about the eye. In at least 347 of the 500 cases there was evidence of local recurrence or metastasis at the time the patients were last seen at the clinic. The majority of these patients have died. In at least thirty-four, or 10 per cent, of the 347 cases there was clinical evidence of melanotic involvement of the central nervous system.

CLINICAL AND PATHOLOGIC CONSIDERATION

In twenty-four cases the brain was the site of the melanomic involvement. In ten cases the spinal cord was affected. In one instance both the brain and the spinal cord were affected. In nineteen of the thirty-four cases the diagnosis was verified by microscopic examination of a specimen removed from the brain or spinal cord at operation or by necropsy (table 1). In the remaining fifteen cases necropsy was not performed or did not include examination of the central nervous system. However, biopsy disclosed that the primary tumor was a melanoma; clinical signs and symptoms were indicative of involvement of the central nervous system and there usually was evidence of generalized metastasis. We have excluded from this study twenty-four additional cases which with but a slight stretch of the imagination might well be included in this category but, because of the absence of postmortem or operative confirmation, must be excluded. It does seem proper to call attention to this additional group because in a study of this type one cannot fail to be impressed by the fact that metastatic involvement of the central nervous system by melanomas is much more common than is generally appreciated. If these twenty-four cases had been included it would have been found that the central nervous system was involved in 20 per cent of the cases of melanoma in which generalized metastasis had occurred. This incidence is less than half of that reported by Courville and Schillinger and by Bailey. This difference may be attributable to our inability to obtain accurate follow-up data.

There are several good reasons for the failure to appreciate the importance of melanotic involvement of the central nervous system. Following a diagnosis of melanoma with evidence of metastases, the patient is frequently taken home and dies without a postmortem examination. Again, in the absence of a primary

melanoma of the skin or in some other obvious site a patient may die without a proper diagnosis and the correct diagnosis may be established only by necropsy, which is performed only occasionally (Plewes). The very late occurrence of metastasis from a primary melanoma may also lead to an incorrect diagnosis. In our series of cases the correct diagnosis would have been overlooked in at least twelve instances had the patient failed to come to operation or necropsy. From these statements it must be appreciated that the statistics on the involvement of the central nervous system by melanoma are rather inaccurate. Twelve of the thirty-four patients died while under observation at the clinic; in ten of the twelve cases necropsy was performed. Seventeen patients died at home; necropsy was performed in four of these cases. The remaining five patients could not be followed.

Of the thirty-four patients, twenty-three were males and eleven were females. Twenty-nine patients are known to be dead and in five cases follow-up data were not available. Necropsy was performed in fourteen of the twenty-nine cases in which death is known to have occurred. In seven of the fourteen cases necropsy was not complete, and in another case, in which necropsy was performed at the patient's home, no mention was made of postmortem examination of the brain or spinal cord. In three of the seven cases neither the brain nor the spinal cord was examined at necropsy and in four cases examination of one of these structures was omitted. Operation was performed in eleven cases, in six for tumor of the brain and in five for tumor of the spinal cord. It is noteworthy that in twelve cases the presence of a melanoma was not suspected prior to operation or necropsy. In eight of the twelve cases no primary melanoma was discovered. In three cases, after the melanoma in the nervous system was found the patient or the family revealed that a mole had been removed previously. In the remaining case the eye had been enucleated some time previously. A diagnosis of glaucoma had been made but because of the subsequent course of events the eye undoubtedly must be considered as the site of a primary melanoma. This group of twelve cases indicates the need of constantly bearing in mind the possibility of a melanoma in the presence of a rapidly progressive disorder of the central nervous system. Great care must also be exercised in the examination of patients suspected of having melanoma and whenever possible any available material should be submitted for microscopic examination.

The ages of the patients at the time of examination at the clinic because of symptoms referable to the central nervous system ranged from 4 years to 66 years. Twenty-two of the thirty-four patients were in the fourth to the sixth decade of life inclusive. The length of time from the excision of the primary melanoma or mole to the death of the patient varied from four months to thirteen years. The average duration was approximately two and a half years. As far as we could determine, the majority of the primary moles had been removed surgically but the mole had been removed some time after evidence of rapid growth had developed. It is pertinent to this problem to insist that moles situated in places subject to irritation should be excised before they show any signs of "wildness." The site of the known primary mole was as follows: back, ten cases; head, face and neck, five cases; eyes, six cases; heel, two cases; hand, one case; umbilicus, one case; labium, one case, and unknown, eight cases. From our studies no definite statement can be made concerning

7. Bailey, Percival: *Intracranial Tumors*, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

8. Dunlap, H. F.: *Metastatic Malignant Tumors of the Brain*, *Ann. Int. Med.* 5: 1274-1288 (April) 1932.

TABLE 1.—*Clinical and Postmortem Data in Thirty-Four Cases of Melanoma of the Central Nervous System*

Case and Sex	Age, Years		Site of Primary Mole	Duration of Neurologic Symptoms Before Visit to Clinic	Clinical Diagnosis	Neurologic Symptoms	Clinical Course	Postmortem Observations	Comment
	When Mole Was Excised	At Death							
1 ♂	39	40	Neck	2½ weeks	Metastatic melanoma of brain	Headache, diplopia and progressive delirium for 2½ weeks; no papilledema	Died 5 days after registration	Multiple melanomas of brain; largest tumor in left temporal lobe; generalized metastasis to organs of body	
2 ♂	..	61	Back	2 months	Melanoma not suspected	Mental confusion and progressive weakness for 2 months; terminal coma; papilledema	Died 3 days after registration	Brain not examined; melanoma in spinal meninges; generalized metastasis to organs of body	Mole not discovered until after death
3 ♀	33	36 (?)	Back	4 months	Metastatic melanoma of brain	Headache, weakness and confusion for 4 months; papilledema of 3-4 diopters	Returned home after operation; condition became progressively worse; no final information	Operation disclosed melanoma of left frontal lobe
4 ♂	62	63	Heel	6 weeks	Metastatic melanoma of brain	Dizziness, vomiting and ataxia for 6 weeks; terminal stupor; no papilledema	Died 2 weeks after registration	Multiple melanomas of cerebrum and cerebellum; spinal cord was not examined; generalized metastasis to organs of body	
5 ♂	41	43	Eyelid	6 months	Melanoma not suspected	Deafness, headache, vomiting and ataxia for 6 weeks; no papilledema	Returned home and died 1 year later	Operation disclosed melanoma of left frontal lobe; mole on eyelid was not recorded in history
6 ♂	..	55	?	1 day	Melanoma not suspected	Left hemiplegia developed gradually 10 days after an exploratory laparotomy	Patient died of cerebral thrombosis (?) 10 days after operation	Multiple melanomas in cortex and ventricles; generalized metastasis to organs of body; site of primary tumor unknown	Exploratory laparotomy disclosed a melanoma
7 ♀	37	?	?	8 months	Melanoma not suspected	Fatigue, headache, falling vision, incoordination and mental dulness for 8 months; papilledema of 5 diopters	Died one day after craniotomy	One large melanoma of left frontal lobe; primary in brain (?); no melanomas in other organs	
8 ♂	..	49	?	7 months	Melanoma not suspected	Signs and symptoms of compression of spinal cord at first thoracic segment for 7 months	Returned home and died 2 months later	Laminectomy and biopsy disclosed a melanoma
9 ♂	38	41	Back	2 months	Melanoma not suspected	Numbness of right arm for 2 months; this was followed by jacksonian convulsions; coma for 4 days before death	Patient died of bronchopneumonia 24 hours after admission	Melanoma (5 cm.) in left parietal lobe; ependymoma of fourth ventricle; melanomas in other organs	History of primary mole not obtained until after necropsy
10 ♂	..	34	?	8 years (?)	Melanoma not suspected	Hemangioma of the cervical segment of the spinal cord suspected and exploratory operation performed 9 months before patient came to clinic; symptoms had progressed; no spinal subarachnoid block; examination of spinal fluid disclosed 50 mg. of protein per 100 cc. and 56 lymphocytes per cubic millimeter	Patient died at home	Another exploratory operation on cervical segment of spinal cord disclosed a melanoma; 4 months later an exploratory laparotomy at home revealed multiple melanomas
11 ♂	..	31	?	2½ months	Melanoma not suspected	Increasing headache, blurred vision and syncope attacks for 2½ months; papilledema of 4 to 6 diopters; no localizing signs	Died 1 day following exploratory craniotomy	Large melanoma of third ventricle, which extended to the fourth ventricle, pons and medulla; only the head examined	
12 ♂	66	67	Eye	3 months(?)	Metastatic melanoma of brain	Headache and weakness following enucleation of eye for melanoma; local recurrence of the tumor; no neurologic examination	Died 2 days after admission	Melanoma of right occipital lobe; extension to arachnoid and dura; generalized metastasis to organs of body	
13 ♂	17	19	Neck	4 months	Metastatic melanoma of brain	Headache, spells of unconsciousness and diplopia for 4 months; papilledema of 5 to 6 diopters	Condition became worse after patient went home; patient died 6 months later	Melanoma removed from left frontal lobe
14 ♂	..	63	?	4 years	Melanoma not suspected	History of progressive lesion of spinal cord for 4 years; partial spinal subarachnoid block; 100 mg. of protein per 100 cc. of spinal fluid	Was alive 2 years after operation; final follow-up data not obtained	Laminectomy and biopsy disclosed a melanoma
15 ♀	..	55	?	3 years	Melanoma not suspected	History of progressive compression of spinal cord at level of fifth thoracic segment; complete spinal subarachnoid block; 1,200 mg. of protein per 100 cc. of spinal fluid	Condition of patient was critical 4 months after she returned home	Laminectomy and biopsy disclosed a melanoma
16 ♀	..	16	?	6 weeks	Melanoma not suspected	Headache, vomiting and papilledema of 4 to 5 diopters for 6 weeks	Died 1 year later at home	Exploratory operation and biopsy disclosed melanoma of cerebellum
17 ♀	40	44	Umbilicus	5 months	Metastatic melanoma of brain	Headache, mental cloudiness and spells of unconsciousness for 5 months; no papilledema	Returned home and died 10 days later	Single melanoma, 3 cm. in diameter, in left parietal lobe; spinal cord not examined; no pathologic report of melanomas in other parts of body	Biopsy at home had revealed that mole was benign; biopsy of lymph node disclosed melanoma

TABLE 1.—Clinical and Postmortem Data in Thirty-Four Cases of Melanoma of the Central Nervous System—Continued

Case and Sex	Age, Years		Site of Primary Mole	Duration of Neurologic Symptoms Before Visit to Clinic	Clinical Diagnosis	Neurologic Symptoms	Clinical Course	Postmortem Observations	Comment
	When Mole Was Excised	At Death							
18 ♂	55	56	Eye	3 months	Metastatic tumor of spinal cord and brain (?)	Eye had been enucleated 9 months previously for glaucoma (?); no pathologic examination; severe facial pain with anesthesia for previous 3 months; signs of compression of spinal cord for 6 weeks; partial spinal subarachnoid block; spinal fluid yellow; 1,600 mg. of protein per 100 cc. of spinal fluid	Returned home and died 3 months later	Generalized melanomas in organs of body; brain and spinal cord not examined	Laminectomy and biopsy disclosed a melanoma
19 ♂	32	33	Eye	6 weeks	Melanoma not suspected	Eye had been enucleated 1 year previously; no pathologic examination; general weakness, absence of knee jerks and attacks of coma for 6 weeks	Condition gradually became worse; patient died 3 weeks after registration	Multiple small melanomas of meninges and bones of skull; generalized metastasis to organs of body	
20 ♂	37	44	Conjunctiva	6 weeks	Metastatic melanoma of brain (?)	Headache, vertigo, incoordination and mental cloudiness for 6 weeks; papilledema; roentgenogram of thorax disclosed metastatic lesions	Returned home and died 2 weeks later	Course of roentgen therapy to head
21 ♀	54	59	Heel	5 months	Metastatic melanoma of brain (?)	Progressive mental change, weakness of left side and left homonymous hemianopia for 6 months	Returned home and died 1 month later	No treatment at clinic
22 ♂	49	55	Scalp	6 weeks	Metastatic melanoma of brain (?)	Progressive weakness of left arm for 6 weeks; blurred vision and vomiting occurred later	Follow-up data not available	No treatment at clinic; 3 small melanomas on left choroid
23 ♂	42	45	Back	3 months	Metastatic melanoma of spinal cord (?)	Lumbar root pain for 3 months; transverse myelitis	Returned home and died 3 months later	Symptomatic treatment
24 ♂	61	63	Nose	3 weeks	Melanoma of spinal cord (?)	Increasing back pain and progressive weakness for 3 weeks	Returned home and died 3 months later	Generalized melanoma of organs of body; vertebral column and spinal nerves involved; brain and spinal cord not examined	Symptomatic treatment at clinic
25 ♀	14	24	Back	3 months	Metastatic melanoma of brain (?)	History of headache; increasing confusion, choked disks and coma for 3 months	Died 2 days after registration	
26 ♂	42	43	Back	6 weeks	Melanoma of spinal cord (?)	Increasing numbness and weakness of legs for 6 weeks	Returned home and died 6 weeks later; transverse myelitis	No treatment at clinic
27 ♀	4	4	Eye	2 months	Metastatic tumor of brain (?)	Enlargement of globe of left eye for several months; enucleation of eye; headache and pain in legs developed later	Mass developed on occiput; patient failed gradually and died at home 2 months after registration	Radium applied to left orbit
28 ♂	52	53	Back	4 weeks	Metastatic melanoma of brain (?)	Headache, progressive aphasia and weakness for 4 weeks; roentgenogram of thorax suggested metastatic involvement	Patient returned home; no follow-up data	No treatment at clinic
29 ♀	45	46	Labia	4 weeks	Metastatic melanoma of brain (?)	Progressive aphasia and generalized weakness for 4 weeks; coma	Died following symptomatic treatment for 2 weeks	
30 ♀	50	54	Back	6 months	Metastatic melanoma of spinal cord (?)	Progressive weakness of left arm for 6 months; roentgenograms disclosed metastatic involvement of thorax and spinal column	Returned home and died 3 months later	No treatment at clinic
31 ♂	60	63	Thumb	6 months	Metastatic melanoma of spinal cord (?)	Progressive back pain with extension to scatic region for 6 months; roentgenogram showed metastatic involvement of sacrum	Returned home and died 6 months later	No treatment at clinic
32 ♂	40	41	Face	5 weeks	Metastatic melanoma of brain (?)	Progressive weakness of left arm for 5 weeks; several jacksonian convulsions; metastatic involvement of thorax	Progressive coma and death	Generalized metastasis to organs of body; brain and spinal cord not examined	
33 ♀	25	27	Back	7 weeks	Metastatic melanoma of brain (?)	Increasing headache, diplopia and vomiting for 7 weeks; rigidity of neck; choked disks of 4 to 5 diopters; metastatic involvement of thorax	Patient returned home and died 4 weeks (?) later	No treatment at clinic
34 ♂	25	35	Back	Metastatic melanoma of brain (?)	Mole removed from back 1 year before registration; generalized melanin pigmentation for 2½ months; melanin in urine	Returned home; had several convulsions; died 4 months later	Necropsy at home; generalized metastasis but no statement about central nervous system	Lead treatment

the presence of other moles. The length of the time the mole was present before removal varied from one to thirty-eight years. A few patients stated that the mole had always been present. As a rule some fourteen months had elapsed between the removal of the initial mole and the first signs of metastasis. Unfortunately we have no definite information regarding the many moles which may have been removed without development of metastases at some later date. As can be seen from table 1, a fair percentage of our patients apparently had an involvement of the central nervous system by melanoma prior to involvement of the other organs of the body. If organs other than the central nervous system were involved first, subsequent involvement of the central nervous system, if it did develop, usually occurred in about two months. In four of the thirty-four cases the primary melanoma occurred in the choroid of the eye. It is interesting to note that during the ten year period under consideration there have been observed at the clinic 125 cases of melanoma of the eye in which enucleation was performed either here or elsewhere. Strangely enough, our figures are not in keeping with those of some of the other writers who maintain that melanoma of the eye is especially prone to metastasize to the central nervous system. Had we been able to obtain follow-up data in the entire group of 125 cases of melanoma of the eye we probably would

TABLE 2.—Results of Examination of Cerebrospinal Fluid in Five Cases of Melanoma of the Spinal Cord

	Case 8	Case 10	Case 14	Case 15	Case 18
Total protein, mg. per 100 cc.	50	100	120	1,200	1,000
Color or transparency.....	Clear	Clear	Yellow	Yellow	Yellow
Spinal-subarachnoid block....	...	Partial	Partial	Complete	Partial

have discovered more than four instances of involvement of the central nervous system, but apparently the percentage is relatively small. Our observations are in keeping with those of Benedict,⁹ who said that melanoma of the choroid tends to metastasize to other organs of the body, especially the liver, in preference to the central nervous system. Terry and Johns,¹⁰ in a review of ninety-eight cases of melanoma of the eye, noted that the diagnosis was incorrect in forty-two instances. The diagnosis in these forty-two cases was glaucoma, opaque cornea, inflammatory lesion and so on and the correct diagnosis was made only by biopsy.

In only one of the thirty-four cases in our series was there metastatic involvement of both the brain and the spinal cord. In three cases the melanoma appeared to be primary in the brain and in three cases it appeared to be primary in the spinal cord. In these six cases operation was performed and the diagnosis of melanoma was made by biopsy. Four of the six patients are known to have died. A complete necropsy was possible in one case and partial necropsy was performed in another case. Two of the six patients were alive at the time the last follow-up data were obtained. In none of these six cases did any signs of metastasis develop. In the case in which complete necropsy was possible the primary melanoma undoubtedly involved the central nervous system. In the other five cases (one of which was reported previously by one of us¹¹) the available data certainly suggested that the primary melanoma involved the central nervous system.

In eleven of the twenty-four cases of melanoma of the brain the outstanding clinical symptoms, such as mental dulness, confusion, coma and delirium, pointed to involvement of the brain. As emphasized by Craig and one of us¹² the neurologic diagnosis may present various difficulties because of the mental status of the patient and the diffuse character of the symptoms. In two cases the clinical picture was confused by the presence of a bromide psychosis or drug intoxication. Several of the patients were moribund when they were brought to the hospital and the correct diagnosis was made only at necropsy. The cerebrospinal fluid was examined in three cases of melanoma of the brain. In two cases the fluid was entirely normal. In the remaining case the value for the total protein was 50 mg. per hundred cubic centimeters of fluid and there were sixty-seven lymphocytes in each cubic centimeter of fluid. The results of examination of the cerebrospinal fluid in five cases of melanoma of the spinal cord are shown in table 2. In no instance was melanin discovered in the spinal fluid.

Roentgenographic examination of the skull was of little value in the diagnosis of melanoma of the brain. In five instances roentgenographic examination of the thorax showed evidence of metastatic involvement and in two additional cases the results of such examination were suggestive of metastatic involvement. Contrary to the usual statement concerning involvement of the bone, we have seen melanotic erosion of the vertebrae, the sacrum and the skull in three cases. Nine of the thirty-four patients showed clinical signs of generalized metastasis when examined at the clinic. Loss of weight was a common symptom. In five cases the sedimentation rates of the erythrocytes were 10, 18, 24, 64 and 109 mm. at the end of one hour, respectively. In only one instance was melanin discovered in the urine, but tests for melanin in the urine were not carried out as a routine in this series of cases.

At times a melanoma may be associated with an acoustic neuroma.¹³ Björneboe¹⁴ has observed the association of melanoma with von Recklinghausen's disease. Occasionally, diffuse melanosis of the skin as reported by Odel and his co-workers¹⁵ (fig. 1) will give the clue to the correct diagnosis. Space will not permit of a lengthy consideration of the individual cases, each one of which presented some interesting diagnostic and clinical problem. The clinical and pathologic data in these cases are shown in table 1.

COMMENT

In considering melanomas it must be emphasized that the frequency of their occurrence in the central nervous system is much greater than is generally recognized. While metastasis usually occurs within a few years after removal of the primary melanoma, as many as ten or even twenty-five years may elapse between removal of a primary melanoma and metastatic involvement of the central nervous system or of other organs of the body. This late development of metastatic melanoma must be kept in mind in any statistical study, for undoubtedly many patients who have melanoma die years after the

9. Benedict, W. L.: Personal communication to the authors.
10. Terry, T. L., and Johns, J. P.: Uveal Sarcoma—Malignant Melanoma: Statistical Study of Ninety-Four Cases, *Am. J. Ophth.* **18**: 903-913 (Oct.) 1935.
11. Da Costa, D. G., and Love, J. G.: Primary Melano-Epithelioma of the Spinal Cord, *Proc. Staff Meet., Mayo Clin.* **14**: 628-631 (Oct. 4) 1939.

12. Craig, W. McK., and Kernohan, J. W.: Melano-Epithelioma of the Brain (Metastatic), *S. Clin. North America* **12**: 989-999 (Aug.) 1932.

13. Bair, H. L., and Love, J. G.: Acoustic Neurofibroma Associated with Melano-Epithelioma of the Choroid: Successful Removal of Both Tumors, *Proc. Staff Meet., Mayo Clin.* **12**: 481-485 (Aug. 4) 1937.

14. Björneboe, M.: Primäres Melanosarkom des Gehirns, massenhafte Naevi pigmentosi der Haut, ausgedehnte Neurofibromatose der Hautnerven, Frankfurt, *Zschr. f. Path.* **47**: 363-373, 1934.

15. Odel, H. M.; Montgomery, Hamilton, and Horton, B. T.: Diffuse Melanosis Secondary to Malignant Melanoma: Report of Case, *Proc. Staff Meet., Mayo Clin.* **12**: 742-747 (Nov. 24) 1937.

removal of the primary mole or melanoma with an incorrect diagnosis. It is of considerable interest, as noted by Knight,¹⁶ Adair and others, that a patient with a melanoma of the eye may survive enucleation of the eye for many years and when metastasis does occur it tends to occur elsewhere than in the central nervous system, especially in the liver. The incidence of metastasis to the central nervous system from melanomas of the eye has been unusually rare in our series of cases as compared to that reported in the literature. One reason for the apparent good prognosis in cases of melanoma of the eye is that the lesion is recognized rather early as a result of the disturbance of vision and the melanoma is removed before extension or metastasis occurs.

It is evident from a survey of our postmortem material that metastatic melanoma may occur throughout the organs of the body without involvement of the central

when a middle-aged person has a rapidly progressing mental or nervous disease and the usual conditions such as vascular disease, inflammatory affliction may be ruled out, it is important to consider seriously the possibility of melanoma of the central nervous system.



Fig. 1.—Diffuse melanosis of skin.

nervous system, and, similarly though to a lesser degree, the brain or spinal cord may be the only site of metastatic involvement.

As noted by Courville and Schillinger, Plewes and others, involvement of bony structures by melanoma has been comparatively rare. When it has occurred it invariably has resulted from direct extension of the melanotic growth. In an appreciable number of cases we have witnessed involvement of the brachial plexus and lumbosacral plexus by melanotic extension or by metastasis.

In the differential diagnosis of melanoma it must be remembered that the patient or relatives frequently will fail to mention the previous removal of a mole. As a rule, such information is withheld unintentionally but in a few cases in our series the knowledge of a mole was deliberately withheld because of the previous unfavorable prognosis. As has been emphasized by Bailey,

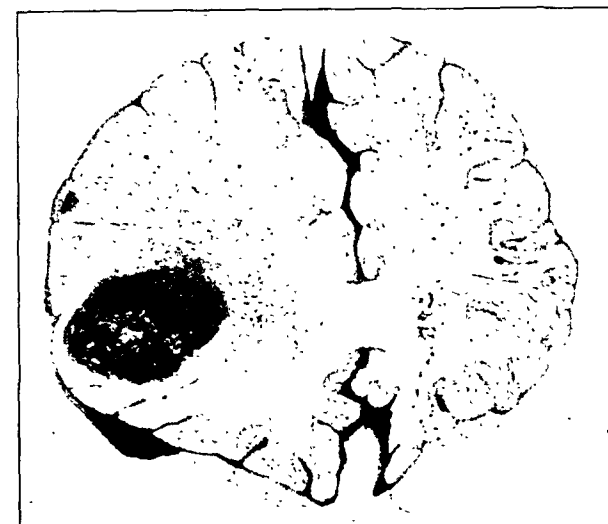


Fig. 2.—Melanoma of brain.

Although at present there seems little that can be accomplished by operation in cases of melanoma of the central nervous system, one should not adopt a defeatist attitude with regard to this serious affliction. In a small percentage of cases a great deal of palliative relief, even if not actual cure, can be obtained by radical operation. If the melanoma is primary in a so-called silent area of the brain, radical surgical removal may be justified; if the lesion is single and nodular, even though metastatic, complete removal may be possible. If the lesion cannot be extirpated from the brain (fig. 2) a palliative subtemporal decompression may afford relief from the increased intracranial pressure and its consequent headache, vomiting and failing vision.

If the melanoma is intraspinal and does not invade the spinal medulla (fig. 3), complete removal is pos-

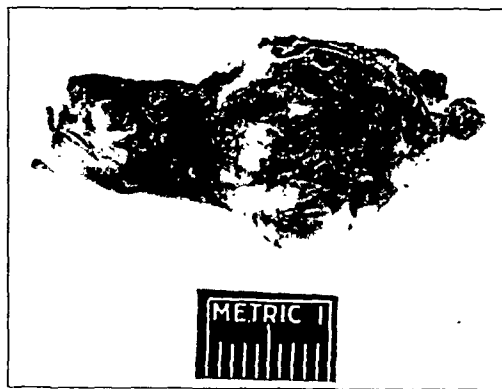


Fig. 3.—Melanoma of spinal cord.

sible. Even if it involves one or more nerve roots, these might be sacrificed in a radical surgical procedure without endangering the patient's life. If the spinal cord or intraspinal nerve roots are involved by a neoplasm, and if the tumor is not too extensive, a subtotal removal is not only justifiable but definitely indicated to ameliorate the patient's symptoms.

16. Knight, Mary S.: Melanotic Neoplasms of the Eye, J. A. M. A. 83:1062-1068 (Oct. 4) 1924.

We do not wish to enter into a discussion of the microscopic appearance of melanomas, but there are several points worth considering. It is generally considered by pathologists that nonpigmented or sparsely pigmented melanomas are more malignant than those deeply laden with pigment. When a nonpigmented melanoma is found by the neurosurgeon it is very difficult for him or the pathologist to identify the origin of such a tumor. The melanin content of many of these neoplasms varies from one region to the next and at times it varies in degree in the same metastatic nodule.

These tumors may spread either by blood stream or by lymphatics and usually by both; the original tumors have a tendency to invade blood spaces early and this explains their wide dissemination throughout the body. It is difficult to understand why in some cases there may be a latent period of many years between the excision of the original tumor and the appearance of the secondary masses. This late recurrence of metastasis is misleading and disconcerting to all concerned in dealing with the problem.

It has been shown in a sufficient number of instances that melanomas arise primarily from the meninges. Before one can accept such a case one must be certain that no small primary skin tumor has been overlooked and that there is no metastasis to other organs. The latter requirement is at times extremely difficult to fulfill on clinical and roentgenologic grounds alone, and without a thorough search at necropsy such a case should be accepted with reservation. In six cases in our series we were of the opinion that the tumors occurred primarily in the central nervous system but because of lack of necropsy we can only say that they possibly originated in the meninges. We were able to prove to our own satisfaction that one tumor was primary in the central nervous system.

CONCLUSIONS

1. Melanoma of the central nervous system is a diagnosis that must be reckoned with by the neurologist.
2. Careful inquiry about the removal of pigmented lesions should be carried out and, if possible, any available material should be reexamined for the presence of melanoma.
3. It must be realized that a melanoma occasionally may be primary in the central nervous system and that in the presence of any rapidly progressive lesion of the central nervous system such a diagnosis must be seriously considered.
4. While it is not in the realm of the neurologist to advise patients regarding lesions of the skin, the opportunity of preaching prophylaxis in the presence of pigmented moles must not be overlooked.

ABSTRACT OF DISCUSSION

DR. S. BERNARD WORTIS, New York: Dr. Moersch and his associates have emphasized the serious nature of melanoma of the central nervous system. Some years ago we reported several from the Bellevue Hospital and can only confirm the observations of Dr. Moersch and his group. Our patients were all over 50 years of age. Papilledema was common. In some of our patients the cerebrospinal fluid was bloody and in a few we were able to find melanin pigment or melanin cells in the spinal fluid. One point worthy of emphasis is that the time between the onset of original irritation of the melanotic focus and the onset of cerebral symptoms varies from eight to ten years, whereas the time elapsing from the onset of cerebral symptoms to death is much shorter, in our series from seven days to two or three months. Many of the symptoms are those referable to disseminated lesions in the nervous sys-

tem simulating diffuse meningo-encephalopathy. Since a third of all melanomas originate in the choroid of the eye, a syndrome can be established wherein one can distinguish four clinicopathologic stages in the course of such tumors. The first stage consists of detachment of the retina by the melanotic tumor and is associated with impairment of vision, a defect in the visual field or complete blindness of one eye. The second stage consists of the period of increasing intra-ocular tension associated with pain. This condition of the eye often resembles glaucoma. However, it can be differentiated from glaucoma by the fact that melanomasarcoma is preceded by blindness and the patient subsequently has pain. In glaucoma pain comes first and blindness is a subsequent occurrence. Subsequent stages give evidence of diffuse involvement of other organs. When the liver is involved in these people the urine gives a positive test for melanuria. I agree with Dr. Moersch and his group that these people require early treatment of the primary focus, and this caution cannot be overemphasized.

DR. PETER BASSOE, Chicago: A man whom I saw when he was 40 years old was known to have had syphilis, had been treated for many years and had become Wassermann negative and was in perfect health until two weeks before I saw him, when he was taken with headache and vomiting, followed by a convulsion and aphasic disturbance. A lumbar puncture was made. The Wassermann reaction was negative with spinal fluid and blood. A few days after the onset I was told that his eyegrounds had been examined in the morning and found normal. In the evening of the same day there were hemorrhages in both eyes; and when I saw him there was a marked papilledema with hemorrhages. We disregarded the syphilitic history and made a diagnosis of tumor of the brain. The patient lived only a few days. Autopsy revealed a large melanotic tumor on the left side, which accounted for the focal symptoms and two other similar tumors which confirm Dr. Moersch's statement that nothing can be done surgically with these tumors. Aside from the vomiting, which undoubtedly was due to the brain lesion, this man had never had anything to call attention to his abdomen. The autopsy, which was complete, showed that the primary tumor was a melanotic carcinoma of the pancreas.

DR. HANS H. REESE, Madison, Wis.: I believe that melanoma belongs to the large group of von Bogaert's congenital neuroectodermal dysplasias: (1) tuberose sclerosis, (2) neurofibromatosis of von Recklinghausen, (3) angiomas and (4) ectodermal dystrophies (xeroderma idiocy, hereditary familial keratoses, congenital generalized ichthyosis). I wish to ask the authors whether or not they considered the melanoma as a subdivision of the status pigmentatus. Von Bogaert of Antwerp is correct in assuming that the various groups are one and the same group but with different tissue selectivity. If the tissue selectivity occurs in the form of a skin melanoma there may be a disturbance in the melanin and iron containing pigment distribution; therefore a radical surgical intervention would remove only a localized metabolic dysplasia of the melanic pigment. I can't see any reason to interfere surgically with a skin lesion. I do not know whether the authors meant that all primary melanomas should be operated on early. Clinical observation reveals that melanomas grow or metastasize with rapidity on intervention. One cannot make the diagnosis of generalized tissue melanoma. Do you consider a melanoma as being a melanomasarcoma or do you regard a localized melanoma only as a specific pigment accumulation in the ectoderm? The various infiltrations of leukemia or of xanthoma do not cure the basic disturbances even if localized lesions are removed. Do you know whether any spectrolytic observations are known which support an early diagnosis of suspected melanoma and which would eliminate a biopsy? Did you find in your post-mortem examinations any increased pigmentations in the globus pallidus, rubra zone, substantia nigra and locus coeruleus? I should like Dr. Moersch to answer the question How do you treat a localized melanoma especially in view of the high probability of metastases?

DR. FREDERICK P. MOERSCH, Rochester, Minn.: The remarks of Dr. Wortis regarding melanoma of the eye are well taken. It is interesting how frequently melanomas of the eye will

metastasize to the liver and not to the brain. As Dr. Bassoe pointed out, many of these patients come in with a very short history. As a matter of fact, some of our patients were brought into the hospital in a state of coma, and not until postmortem examination was the melanoma discovered. In the paper I purposely avoided the possibilities that Dr. Reese suggested because I believe it becomes an exceedingly controversial subject as to what one man considers a melanoma and what is considered melanoma by another. I am sorry Dr. Kernohan is not here to answer the questions of Dr. Reese. I am sorry I cannot.

A PREPARATION OF TOXIN SUITABLE FOR ORAL IMMUNIZATION AGAINST SCARLET FEVER

GEORGE F. DICK, M.D.

AND

GLADYS HENRY DICK, M.D.

CHICAGO

That sterile scarlet fever toxin administered by mouth may result in satisfactory immunization was reported in 1932.¹ This observation was first made during attempts to learn whether or not some of the so-called intestinal rashes mentioned as occurring in children might be caused by milk which had been contaminated with a scarlet fever streptococcus and subsequently pasteurized at a temperature which kills the streptococci but does not destroy the toxin.

In these first experiments it was found that transient scarlatinal rashes might occur in susceptible persons when comparatively large doses of the sterile toxin were ingested. Subsequent cutaneous tests showed modification of the susceptibility, indicating the production of some degree of antitoxic immunity.

This observation led to further experiments in which sterile toxin, containing 0.5 per cent phenol, was administered by mouth in graduated doses. The results indicated that, if enough toxin was given, a degree of immunity sufficient to protect against an attack of scarlet fever was obtained. But, as might be expected, the amount of toxin required to produce immunity, when administered by mouth, was many times the amount which produced comparable immunity when injected subcutaneously.

During the next several years, while experiments were being made to improve the method, immunization by mouth was limited to use in special cases, such as persons in whom hemophilia or severe cardiac lesions had been diagnosed or in institutions under quarantine for scarlet fever when speed in immunization was a prime consideration. It was also occasionally employed in highly susceptible individuals as a preliminary treatment to establish some immunity before hypodermic injections were begun, or in persons so highly sensitized to proteins contained in peptone that hypodermic injections of the toxin resulted in urticaria.

For obvious reasons, commercial distribution of undiluted fluid scarlet fever toxin in 1 liter volumes to be taken by mouth was not practical. It was apparent that it would be desirable to obtain the toxin in a more compact form and, if possible, in a dry state. To obtain such a preparation and to purify as well as concentrate the toxin for further chemical study, investi-

gations were undertaken which have resulted in a highly concentrated and comparatively pure toxin in the form of a white powder.

This substance was carefully standardized, and weighed amounts were combined with pure saccharose to make powders containing different numbers of skin test doses of toxin. Given in these powders, the toxin caused more nausea and vomiting than when it was administered in the liquid state as crude toxin. We concluded that the reason for this difference was that the dry toxin remained in the stomach longer than when it was given in solution.

In an attempt to overcome this difficulty, the toxin was prepared in a saccharose syrup which the children found agreeable but which also caused more nausea than the hypodermic injections, though considerably less than the powders. Probably because of the loss of toxin through vomiting, the powders did not immunize. The syrup, causing less vomiting, produced satisfactory immunity.

In order to eliminate as far as possible nausea with resultant discomfort and sometimes loss of toxin, we decided to try protection of the toxin from absorption in the stomach. Enteric sealed capsules and enteric coated tablets were prepared. Of these two forms the tablets proved easier for small children to swallow. With the cooperation of one of the manufacturers, a number of enteric coated tablets were prepared from the purified toxin. These tablets were made in three strengths: a hundred thousand, one million and two million skin test doses per tablet.

There is considerable variation in the solubility of enteric coated tablets on the market. The solubility depends chiefly on four factors: the kind of substance used for the enteric coating, the thickness of coats applied, the rate of solution of the outer, decorative coat and the motility of the alimentary tract. In persons who have bowel movements at intervals of two or three days the chance of absorption is naturally better than in persons who eliminate residue of food in less than twenty-four hours after ingestion. We have found the standard chemical tests for solubility less satisfactory than actual feeding of the tablets under consideration along with an insoluble tablet, to serve as a marker, to persons known to have a habit of rapid elimination, and searching the stool which contains the marker for other undissolved tablets.

The use of tablets which do not dissolve prevents immunization, while the feeding of tablets that permit release of toxin in the stomach results in vomiting such as occurred when the powdered toxin was introduced directly into the stomach.

Tablets have been employed in the immunization of 131 persons susceptible to scarlet fever. With the exception of one case in this series, the reactions have not been recorded by us but by doctors or nurses in immediate charge of the groups or individuals, and the charts returned when the work was completed. The largest single group comprises fifty-four students at Berea College, where the immunization was supervised by Dr. Armstrong.

Preliminary skin tests were made in every case, and the size and intensity of the reaction were recorded. The skin test was repeated two weeks after completion of the immunization with the exception of one small group which there was no opportunity to retest until two months had elapsed. In the retests, one skin test dose of toxin was injected on the right forearm and two skin test doses on the left forearm. The immuni-

Read in the panel discussion on Some Contagious Diseases before the Section on Pediatrics at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Dick, George F., and Dick, Gladys Henry: Antitoxic Immunity Resulting from Administration of Toxin by Mouth, *J. A. M. A.* 98: 1436 (April 23) 1932.

zation is not considered complete unless the cutaneous reaction to two skin test doses of toxin is negative at the time of retest shortly after completion of the doses.

Preliminary experiments directed toward determining the effective dosage indicated that, while some persons became immune with smaller amounts, the average total dosage should approximate seventy-five million skin test doses of toxin given over a period of three weeks. The tablets were taken immediately after meals, beginning, in most cases, with one hundred thousand skin test doses and gradually increasing to six or ten million skin test doses a day for the last three to six days. No modification of dosage was made on account of age. The series included individuals from 1 to 36 years of age.

In twelve persons the dosage was not carried above one to four million skin test doses a day. All but two in this group showed modified but positive cutaneous reactions on retest.

One group received improperly coated tablets which would partially dissolve in the stomach. In this group, vomiting and diarrhea were frequent complaints. Of the seventeen who completed the course of tablets, eleven, or 64.7 per cent, were immunized. Those who complained of diarrhea, so that they were less apt to absorb the toxin, acquired the least immunity.

Of the 102 persons of various ages who received better toxin tablets in amounts ranging from forty-seven to ninety-one million skin test doses distributed in graduated amounts over a period of two to three weeks, 94.7 per cent were immune on retest. In four cases, or 3.8 per cent, transient scarlatinal rashes occurred at some time, usually on the day four million skin test doses of toxin were given. Two persons vomited once.

With the more gradual increase in dosage in use during the past six months, and stricter control of the solubility of the tablets, reactions have been reduced to an occasional "stomach-ache" of short duration.

The series includes six persons who were so highly sensitized to the proteins contained in peptone that hypodermic injections were considered inadvisable. Their immunization by mouth was successful and uneventful. The further observation was made that, during the course of oral immunization, they became at least partially desensitized to peptone.

Results of further clinical experiments have shown that, whatever type of enteric coating is used, it is necessary to regulate the dosage of scarlet fever toxin according to the rate of disintegration or solution of the tablet. Immunization may be accomplished with doses of toxin smaller than those employed in the first experiments. In instances in which enteric coatings that permitted disintegration of the tablets within three hours in physiologic solution of sodium chloride buffered at p_H 7.0 were employed, the maximum daily dosage required to produce immunity was reduced to one to three million skin test doses of toxin.

It is not suggested that oral administration of toxin be generally substituted at this time for the present method of shallow hypodermic injections of sterile toxin in graduated doses. There are, however, definite advantages in the oral route in the conditions mentioned in the first part of this paper, the additional advantage that it lends itself more readily to modification according to the reactions of the individual patient and that immunization may be accomplished in a shorter time with fewer reactions.

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INTRAVENOUS USE OF 2-METHYL-1,4-NAPHTHOQUINONE IN HYPO-PROTHROMBINEMIA

CLINICAL OBSERVATIONS

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AND

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The isolation and synthesis of vitamin K_1 (2-methyl-3-phytyl-1,4-naphthoquinone) in August of 1939 by Fieser and his associates,¹ by Doisy and his co-workers² and by Almquist and Klose³ gave new impetus to the clinical evaluation of the antihemorrhagic activity of synthetic vitamin K_1 and its chemical derivatives in hypoprothrombinemia. It has been amply established by Ansbacher and his associates⁴ and by others⁵ that 2-methyl-1,4-naphthoquinone and more recently that 2-methyl-1,4-naphthohydroquinone are more rapidly acting and have greater potency than the many other derivatives of vitamin K_1 thus far elaborated in the biochemist's laboratory.

It is our purpose in this paper to report our experience with the intravenous use of 2-methyl-1,4-naphthoquinone for patients suffering from hypoprothrombinemia.

CHEMISTRY

Numerous chemical compounds closely related to the naturally occurring vitamin K_1 of alfalfa and K_2 of putrefied fish meal have been made available for clinical research, and certain facts have been established. Those compounds containing the phytyl group are less rapidly utilized by the animal's body.⁶ The hydroxy group in the 3 position appears to reduce potency,⁷ while the methyl group in the 2 position has been found essential. 2-methyl-1,4-naphthoquinone is a canary yellow crystalline substance, readily soluble in oil and slightly soluble in warm water (1 mg. in 10 cc.). The solution slowly loses potency on exposure to light but retains its activity in a dark refrigerator for several days. We have used 2-methyl-1,4-naphthoquinone exclusively in this study.

TOXICITY

Molitor and Robinson⁸ determined the acute and chronic toxicities of 2-methyl-1,4-naphthoquinone on mice, rats and chicks. They found a very large safety

From the Department of Internal Medicine, the Lahey Clinic.

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2. Binkley, S. B.; Cheney, L. C.; Holcomb, W. F.; McKee, R. S.; Thayer, S. A.; MacCorquodale, D. W., and Doisy, E. A.: The Constitution and Synthesis of Vitamin K_1 , *J. Am. Chem. Soc.* **61**: 2558-2559 (Sept.) 1939.

3. Almquist, H. J., and Klose, A. A.: Synthetic and Natural Antihemorrhagic Compounds, *J. Am. Chem. Soc.* **61**: 2557-2558 (Sept.) 1939.

4. Ansbacher, S.; Fernholz, E., and Dolliver, M. A.: Vitamin K-Active Derivatives of 2-Methyl-1,4-Naphthohydroquinone, *J. Am. Chem. Soc.* **62**: 155-158 (Jan.) 1940; Water Soluble Antihemorrhagic Compounds, *Proc. Soc. Exper. Biol. & Med.* **43**: 652-655 (April) 1940.

5. Butt, H. R.; Snell, A. M.; Osterberg, A. E., and Bollman, J. L.: Treatment of Hemorrhage by the Use of Various Synthetic Compounds, *Proc. Staff Meet., Mayo Clin.* **15**.

6. Almquist, H. J., and Klose, A. A.: The Antihemorrhagic Activity of Pure Synthetic Phthiocol, *J. Am. Chem. Soc.* **61**: 1611 (June) 1939.

7. Almquist, H. J., and Klose, A. A.: The Antihemorrhagic Activity of Pure Synthetic Phthiocol, *J. Am. Chem. Soc.* **61**: 1611 (June) 1939.

8. Molitor, H., and Robinson, H. J.: Oral and Parenteral Toxicity of Vitamin K_1 , Phthiocol and 2-Methyl-1,4-Naphthoquinone, *Proc. Soc. Exper. Biol. & Med.* **43**: 125-218 (Jan.) 1940.

TABLE 1.—Response to Treatment

Prothrombin Time in Percentage of Normal																				
Case	Diagnosis	Jaundice	Bleeding	Liver Function	Dose of 2-Methyl-1,4-Naphthoquinone	Before Treatment	After Treatment													Results
							2 Hr.	4 Hr.	6 Hr.	12 Hr.	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	
1	Portal cirrhosis; subacute yellow atrophy	+	+	80% retention of bromsulphalein	2 mg.	67	55	59	73	..	Died	Poor; very slight effect from oral or intravenous medication
2	Idiopathic stenorrhea	-	-	Takata-Arn +	1 mg., repeated in 24 hours	62	65	63	Dose repeated	71	100*	Good response to 24 mg. dose
3	Carcinoma of head of pancreas	+	-	1 mg., repeated in 24 hours	59	68	76	74	73	(24 Hr.) (45 Hr.) (63 Hr.) Dose repeated	100	Transfusion	Good response to 2d mg. dose
4	Biliary fistula	+	+	1 mg.	10	100*	Good (child)
5	Common duct stenosis; biliary cirrhosis	+	+	1.5 mg., followed in 24 hr. by 1 mg., followed in 16 hr. by 2 mg.	33	66	77	58	Died	Poor
6	Carcinoma of bile ducts	+	-	1 mg., repeated in 24 hours	55	73	87	100	Dose (41 Hr.) repeated	..	100	Good
7	Cirrhosis; common duct stone	+	-	Takata-Arn +	2 mg., followed in 24 hr. by 1 mg.	54	41	..	61	..	Dose repeated	Died	Poor
8	Common duct stone	+	-	2 mg.	53	100	100	100	100	Good; prothrombin maintained
9	Biliary fistula	+	-	2 mg.	49	64	73	..	80	100	105	Operation, transfusion	93	..	83	71*	Good
10	Biliary fistula; hepatitis	+	+	Hippuric acid less than 0.11 Gm.	2 mg., repeated in 10 days	62	90	90	..	100	70	83*	Operation	100	Transfusion	Good first response; delayed 2d response after hepatitis developed
11	Carcinoma of hepatic flexure of colon with obstruction	-	+	2 mg.	72	86	100	90	Transfusion	89*	..	Good
12	Jejunal fistula	-	+	2 mg., repeated in 5 days	49	81	..	100	94	70	Dose repeated	Good
13	Hepatitis	+	-	2 mg., repeated in 2 days	80	88	88	80	Dose repeated	86	Fair
14	Biliary fistula	-	+	2 mg.	83	83	87	87	..	95	..	100*	Good
15	Carcinoma of gallbladder; biliary fistula; biliary cirrhosis	+	-	2 mg., repeated in 6 days	58	69	..	69*	69	Dose repeated	85	..	Fair after 2d dose
16	Biliary obstruction by duodenal ulcer	+	-	2 mg.	90	100	98	..	100	Good; prothrombin maintained
17	Common duct stricture; biliary cirrhosis	+	+	2 mg., repeated in 4 days	40	52	..	76	81	89	91	86	Dose repeated	91	87	Good but level not maintained
18	Common duct stricture	+	-	2 mg.	76	70	..	90	100*	Good
19	Common duct stone	+	-	2 mg.	76	80	100	100	1 1/2 days	Good
20	Gastric ulcer; subtotal gastrectomy	-	+	2 mg.	76	92	103	84	Good
21	Cirrhosis; carcinoma of rectum	-	-	2 mg.	70	69	94	94*	Good; slower than usual
22	Carcinoma of head of pancreas	+	-	2 mg.	72	77	100*	19 Hr. 28 Hr.	Good

* Oral medication begun.
† Dose repeated.

factor between the toxic and therapeutic doses; 500 mg. per kilogram of body weight was the L. D. 50 orally in mice with this substance. Chronic toxicity in rats was tested over a period of thirty consecutive days on varying daily doses; 500 mg. per kilogram of 2-methyl-1,4-naphthoquinone was toxic and 350 mg. per kilogram caused a marked fall in red blood cell count and

Prothrombin determinations were made immediately before intravenous treatment was administered and at varying intervals thereafter. We have considered a prothrombin clotting time of 90 per cent or over as normal.

The solution of crystalline 2-methyl-1,4-naphthoquinone¹¹ was prepared by dissolving 10 mg. in 100 cc. of sterile hot physiologic solution of sodium chloride. This was used immediately or was protected from light and stored for short periods of time in the refrigerator. The intravenous injection was made slowly into an ante-cubital vein.

RESULTS

During the seven months between February and September of 1940 we have administered 2-methyl-1,4-naphthoquinone intravenously to twenty-two patients, twenty of whom had hypoprothrombinemia. A brief outline of these cases, together with their response to treatment is presented in table 1. The conditions considered most important in causing the hypoprothrombinemia in each case have been summarized in table 2. Patients 8 and 16 received 2-methyl-1,4-naphthoquinone prophylactically. The response to intravenous treatment was considered good in 17 (77.3 per cent), fair in 2 (9.1 per cent) and poor in 3 (13.6 per cent).

In attempting to establish the minimum effective intravenous dose of 2-methyl-1,4-naphthoquinone in the adult it was demonstrated that although 1 mg. would usually cause a definite rise in the prothrombin level a second milligram dose was needed before a normal prothrombin could be obtained. Patient 4 showed a complete response to 1 mg. intravenously, but this

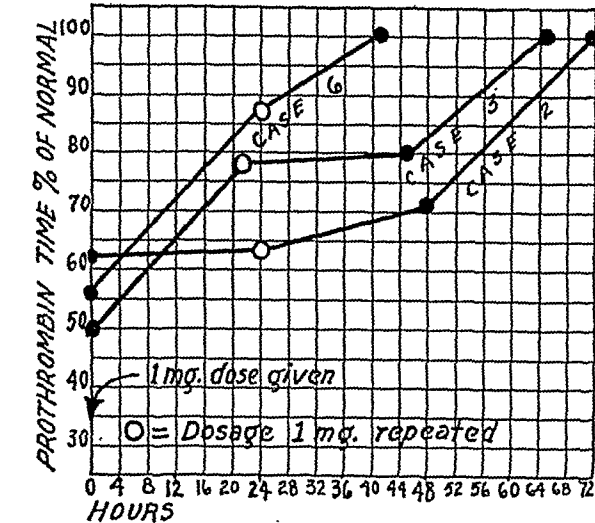


Chart 1.—Effect of 1 mg. intravenous doses of 2-methyl-1,4-naphthoquinone on hypoprothrombinemia.

in hemoglobin. Natural vitamin K₁ did not cause these changes.

In the human being no toxic effect from 2-methyl-1,4-naphthoquinone has been reported when small oral doses were used, but Koller⁹ has described nausea and vomiting following the oral administration of large doses (3 mg. per kilogram of body weight).

METHOD

In this study we have used Quick's¹⁰ method of prothrombin time determination but have reported this

TABLE 2.—Conditions Considered Most Important in Causing Hypoprothrombinemia

	Cases
Common duct obstruction.....	8
Biliary fistula.....	4
Cirrhosis.....	4
Hepatitis.....	1
Subacute yellow atrophy.....	1
Idiopathic steatorrhea.....	1
Subtotal gastrectomy.....	1
Jejunal fistula.....	1
Obstruction of large intestine.....	1
	22

in terms of percentage of normal as suggested by H. J. Perkin of the clinic's research laboratory early in our investigation of vitamin K and related prothrombogenic substances. This method permits minor changes in potency of the thromboplastic substance without affecting the final result in the individual test. The patient's prothrombin time in percentage of normal is calculated by dividing the patient's prothrombin clotting time by the normal control's prothrombin clotting time and multiplying by 100.

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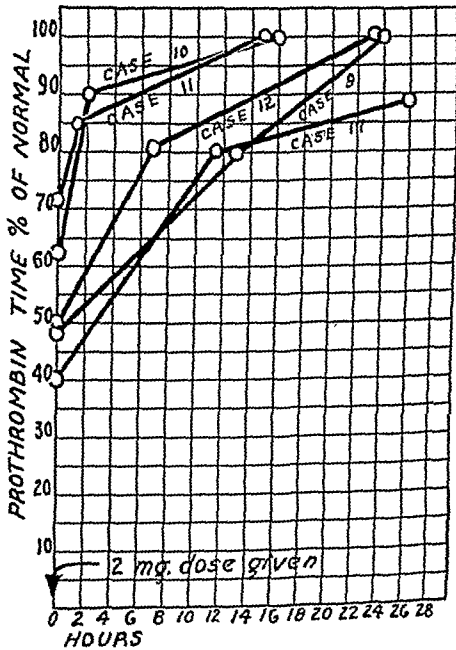


Chart 2.—Effect of 2 mg. intravenous dose of 2-methyl-1,4-naphthoquinone on hypoprothrombinemia.

patient was a 3 year old child. Chart 1 demonstrates the limitation of response to the 1 mg. dose in the adult.

The effect of a 2 mg. dose of 2-methyl-1,4-naphthoquinone intravenously is shown in chart 2. These patients were selected to demonstrate this point because of their initial low levels of prothrombin and because liver damage, with the exception of case 17, was absent or of such degree as not to interfere seriously with the

11. The crystals were supplied to us by E. R. Squibb & Sons.

response. From these results we conclude that some patients may be expected to show beginning effect as early as two hours after receiving intravenous medication, that a prothrombin level of 80 per cent of normal is reached in an average of about seven and one-half hours, and that 100 per cent of normal is attained in an average of about twenty hours.

The duration of the effect of 2 mg. of 2-methyl-1,4-naphthoquinone is shown in chart 3. It is seen that the prothrombin level will remain above 90 per cent of normal for four or more days unless complicated by liver damage. Case 17, in which there was some liver impairment, also appears on the chart and shows a more rapid drop.

We have confirmed the reports of numerous other investigators with regard to the effect of liver damage and have found no increased response in such cases by the intravenous route of administration as compared with the oral route. The patients who responded slowly or incompletely suffered, without exception, from

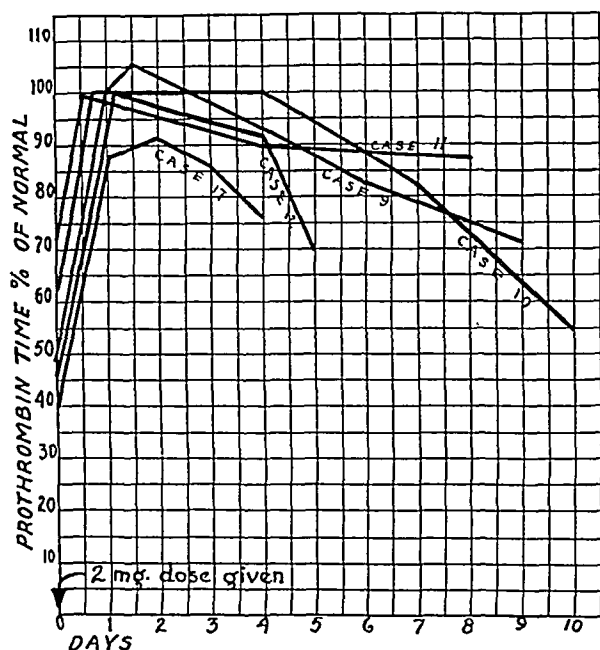


Chart 3.—Duration of effect after 2 mg. intravenous dose of 2-methyl-1,4-naphthoquinone on hypoprothrombinemia.

some degree of liver damage. This was demonstrated in some cases by liver function tests and in others by direct observation of the liver at operation. Severe liver damage was necessary to prevent more than a slight response to intravenous 2-methyl-1,4-naphthoquinone (cases 1 and 7). When the impairment of liver damage was less severe, some initial increase in prothrombin occurred but the response was not complete and the prothrombin clotting time could not be lowered to a completely normal level nor could it be maintained as easily as in those cases in which there was no appreciable liver damage (cases 5, 10, 13, 15, 17 and 21). Repeated intravenous doses in this group sometimes led to more normal levels (case 15).

In nine cases bleeding occurred before the administration of 2-methyl-1,4-naphthoquinone, but bleeding was effectively controlled except in cases 1 and 5, in which severe liver damage existed.

By this route of administration bile salts were not necessary.

Except for the temporary pain near the site of injection in five cases, no toxic effects were noted. In no case could any drop in blood count or hemoglobin level be attributed to this drug.

REPORT OF CASES

We have chosen four illustrative cases to present in detail:

CASE 1.—A man aged 43, a druggist, entered on Jan. 23, 1940, with a story of recurrent jaundice of two years' duration. He had been a heavy drinker for three years before the onset of this condition but had consumed no alcohol in the two years previous to entry. There had been no pain, chills or fever. Roentgenograms taken elsewhere two weeks before entry were said to show a stone in the gallbladder region. Slight epistaxis had occurred occasionally, as well as some bleeding from the gums.

Physical examination showed the scleras to be slightly icteric. The skin was dry and there were a few follicular keratoses on the arms. On the lower legs were several papular, purpuric, pin point lesions. The liver extended from the sixth interspace superiorly to a sharp edge 3 fingerbreadths below the right costal margin. It extended well into the epigastrium and was smooth, firm and slightly tender. The splenic tip descended 2 fingerbreadths below the left costal margin. No ascites could be elicited. There were numerous dilated venules over the lower anterior chest wall bilaterally. There was no peripheral edema.

The patient was sent immediately into the hospital with the diagnosis of biliary cirrhosis and a question of cholelithiasis. Laboratory test showed 15.6 Gm. of hemoglobin (100 per cent Sahli), 5,000,000 erythrocytes and 6,330 leukocytes. The prothrombin time was 65 per cent; the bilirubin showed an indirect reaction and was 2.8 mg. per hundred cubic centimeters. The urobilinogen was positive in 1:256 dilution. The serum protein was 7.5 per cent, the Hinton test was negative and the urine was normal. The icteric index was 45. The Takata-Ara test was strongly positive and 80 per cent of the bromsulphalein was retained after one hour.

The patient was given vitamin B complex by mouth and members of the B complex intramuscularly. He was given 2-methyl-1,4-naphthoquinone orally in 2 mg. doses three times a day, together with bile salts 10 grains (0.65 Gm.) three times a day. At the end of nine days the prothrombin had risen to 75 per cent and at this time natural vitamin K₁ was given orally with bile salts, without any further rise in the prothrombin time.

In spite of the evidence of hepatitis and our inability to raise the prothrombin time to a normal level, an exploration was deemed necessary. This was done February 10. A markedly scarred liver was found, but no stones were felt. The liver biopsy showed a toxic hepatitis with cirrhotic changes.

The patient did poorly after operation. His prothrombin dropped to 53 per cent of normal, and oral 2-methyl-1,4-naphthoquinone, together with bile salts, raised this to 67 per cent of normal.

On the seventh postoperative day the patient began to show evidence of cholemia and uremia and vomited a total of about 6 ounces (178 cc.) of blood. His prothrombin time was 67 per cent of normal, and 2 mg. of 2-methyl-1,4-naphthoquinone was given intravenously. The poor prothrombin response is shown in table 3.

The patient died on the eighth postoperative day. Postmortem examination showed toxic cirrhosis of the liver with a superimposed subacute yellow atrophy, massive gastrointestinal hemorrhage and cholelithiasis with soft stones in the bladder but none in any of the ducts.

CASE 4.—A boy aged 3 years was brought to the clinic on Jan. 31, 1940, because of an abdominal mass present since the age of 12 months and jaundice of two weeks' duration. The parents had been told that the abdominal mass was an enlarged liver. There had been several attacks of cough, anorexia, clay-colored stools, dark urine and general malaise. During these attacks the abdominal mass increased in size, but as the symptoms subsided the mass became smaller and the color of the

stools and urine returned to normal. Jaundice had been present for about two weeks before admission and there had been a mild pruritus for several days.

On physical examination the boy was well developed and well nourished, with moderate pallor of the mucous membranes and a mild icterus of the scleras. There were a few excoriations on the skin of the trunk and legs. A few medium rales were heard throughout both lung fields. Examination of the abdomen

TABLE 3.—Prothrombin Response in Case 1

Date	Prothrombin Time, per Cent	2-methyl-1,4- naphthoquinone
2/17/40 8:45 a. m.	67	2 mg. Intravenously
10:30 a. m.	55	
12:30 a. m.	59	
2:45 p. m.	73	
4:30 p. m.	67	
2/18/40 a. m.	55	

revealed a cystic mass approximately 9 cm. in diameter in the right half of the abdomen. The spleen was not palpated. A few shotty cervical glands were felt. The temperature was 99 F. by rectum, the weight 35½ pounds (16 Kg.) and the height 39½ inches (100 cm.). The rest of the physical examination gave essentially normal results.

The urine on admission showed a trace of bile but was otherwise negative. The bile gradually increased in the urine after entry, the leukocyte count was 11,450, hemoglobin 62 per cent (Sahli), erythrocytes 4,080,000, differential 80 per cent polymorphonuclears, 17 per cent lymphocytes, 3 per cent monocytes. The icteric index was 17 and the hematocrit reading 40. The bilirubin was 1.4 mg. per hundred cubic centimeters. The platelet count was 544,000, the reticulocyte count 1.9 per cent. There was moderate achromia. The stools showed a trace of bile.

After a mild bronchitis had cleared, exploratory operation was performed on February 15. At this time a congenital dilatation of the common bile duct, containing about a liter of bile, was found, and marsupialization of the dilated duct was carried out. The prothrombin clotting time preoperatively was 100 per cent of normal and remained so immediately after operation. Large amounts of bile drained through the catheter which had been placed in the common bile duct and an attempt was made to give the patient bile salts by mouth. This was only partially successful, as he refused this medication on and after March 13. On March 18 the urine began to show many red blood cells in the sediment. On March 21 he became nauseated and vomited several times, was listless and had a fever of 101 F. by rectum in the evening. A hypodermoclysis was given on this date and there was some bleeding from the

TABLE 4.—Prothrombin Response in Case 9

Date	Prothrombin Time, per Cent	2-methyl-1,4- naphthoquinone
5/18/40 9:00 p. m.	49	2 mg. intravenously
10:00 p. m.	51	
11:00 p. m.	64	
12:00 m.	73	
5/19/40 10:15 a. m.	80	
8:00 p. m.	100	
5/20/40 8:00 a. m.	105	

skin wounds after the withdrawal of the needles. The next day, March 22, he bled from the needle wound in the lobe of the ear where blood had been taken. On March 23 bright red blood was passed by rectum and the bleeding continued from the ear lobe and from the nose.

Examination of the blood at this time showed a leukocyte count of 16,000, and the hemoglobin had dropped from 89 per cent on March 1 to 60 per cent. The prothrombin clotting time on March 23 was found to be 10 per cent of normal. At 5 p. m. 1 mg. of 2-methyl-1,4-naphthoquinone, dissolved in 10 cc. of physiologic solution of sodium chloride was given intravenously. By 7 o'clock the same evening all bleeding had stopped, and

eighteen hours after the medication the prothrombin time was 100 per cent of normal.

The patient's clinical condition improved markedly, his temperature fell to normal, his appetite returned and he was again running about the wards. He was then given tiny repeated doses of bile salts and 6 mg. of 2-methyl-1,4-naphthoquinone orally each day. The prothrombin time remained 100 per cent of normal. On March 30, choledochoduodenostomy was performed. The patient was discharged on April 13, with normal colored stools and urine, and with all evidence of jaundice gone.

CASE 9.—A man aged 42, a druggist, admitted on May 17, 1940, had had attacks of epigastric pain during the previous year extending to the right scapular region. Three weeks before entry he had undergone a cholecystectomy elsewhere, at which time several stones were removed. Following this procedure he had become intensely jaundiced, had experienced chills and fever, and had noted dark urine and light colored stools. One week before entry a biliary fistula had developed and the jaundice had partially subsided.

Physical examination was essentially negative except for moderate icterus of the skin and scleras, a palpable liver edge 1 fingerbreadth below the right costal margin and a biliary fistula.

The patient entered the hospital on the same day. The icteric index was 35, the hemoglobin 91 per cent (Sahli), the erythrocytes 5,010,000 and the leukocytes 5,500. The serum bilirubin was 7.8 mg. per hundred cubic centimeters (indirect). May 18

TABLE 5.—Response to 2-Methyl-1,4-Naphthoquinone in Case 10

Date	Prothrombin Time, per Cent	2-methyl-1,4- naphthoquinone
5/10/40 3:30 p. m.	62	2 mg. intravenously
4:30 p. m.	63	
5:30 p. m.	90	
6:30 p. m.	90	
7:30 p. m.	90	
5/20/40 8:00 a. m.	100	

at 9 p. m. the prothrombin time was 49 per cent of normal and at this time 2 mg. of 2-methyl-1,4-naphthoquinone was given intravenously. His prothrombin response is shown in table 4.

On May 21 operation was performed and a transfusion of 500 cc. of citrated blood given. The common duct was found to have been divided and the intrahepatic portion of the common duct was anastomosed to the jejunum. The postoperative course was uneventful. The prothrombin time gradually fell to 71 per cent of normal on May 27, and at this time natural vitamin K₁ and bile salts were started by mouth. On June 6 the prothrombin time had risen to 89 per cent. The patient was discharged markedly improved on June 9, at which time his icteric index was 9 and the bilirubin 0.1 mg. per hundred cubic centimeters (indirect).

CASE 10.—A woman aged 31, a housewife, entered the clinic on May 18, 1940, complaining of the presence of a bile fistula of five months' duration. She had had a cholecystectomy elsewhere in 1931 and in November of 1939 had had a recurrence of right upper quadrant pain. In January 1940 another operation was performed elsewhere and she was told that her common bile duct had "shriveled up." A T tube had been sutured in place and was there on admission to the hospital. At this time there was slight bleeding around the tube.

On physical examination the patient appeared thin and jaundiced and was in no acute distress; she showed general malnutrition and tenderness in the right upper quadrant, where there was a rubber catheter in place.

She entered the hospital immediately and there a urine examination revealed albumin 3+ and bile 2+. The bilirubin was 9.0 mg. per hundred cubic centimeters, the nonprotein nitrogen 21 mg. per hundred cubic centimeters. The leukocytes numbered 11,750, the erythrocytes 3,440,000; the hemoglobin was 66 per cent (Sahli). The differential was normal. The Hinton test was negative. Examination of the stools showed

a 3+ benzidine test for blood and no bile. The prothrombin time was found to be 50 per cent of normal.

The patient was given 2 mg. of 2-methyl-1,4-naphthoquinone intravenously, and the response is shown in table 5.

On May 22 the patient underwent operation, and a stricture at the ampulla of Vater was found. This was dilated and a T tube left in the common bile duct. Four days after operation the prothrombin had fallen to 83 per cent. At this time she was given a transfusion of 250 cc. of citrated blood and on the seventh postoperative day the prothrombin time had dropped to 55 per cent and she started to bleed. At this time she was given another 2 mg. of 2-methyl-1,4-naphthoquinone intravenously, and the prothrombin time was brought up to 83 per cent of normal in two days. All bleeding had stopped five hours after the medication had been given intravenously. At this time she was given natural vitamin K₁ and bile salts by mouth three times a day, and the prothrombin time rose to 100 per cent. On June 19 the T tube was removed. Following this a temperature of 102.4 F. developed and the bilirubin rose to 17.0 mg. per hundred cubic centimeters. On June 21 the prothrombin had dropped to 65 per cent and she again received 2 mg. of 2-methyl-1,4-naphthoquinone intravenously, but the prothrombin time remained low in spite of the fact that the dose of 2 mg. was repeated in twenty-four hours and 1 mg. in forty-eight hours. At this time an intravenous hippuric acid test was less than 0.44 Gm., thus showing marked liver damage, which was thought due to hepatitis.

The fever gradually subsided and the bilirubin dropped to 13 mg. per hundred cubic centimeters. The patient was given 2-methyl-1,4-naphthoquinone and bile acids by mouth. As the evidence of hepatitis subsided the prothrombin gradually rose to 90 per cent in the course of the next four days. She was discharged improved on June 28.

Case 1 demonstrates the ineffectiveness of 2-methyl-1,4-naphthoquinone when severe liver damage existed. Case 4 illustrates the dramatic effect of this drug in bleeding due to hypoprothrombinemia. In case 9 the average response of uncomplicated vitamin K deficiency to 2-methyl-1,4-naphthoquinone, given intravenously, is shown. Case 10 contrasts the effect of 2-methyl-1,4-naphthoquinone in hypoprothrombinemia before, during and after the development of liver impairment.

COMMENT

The value of the prothrombogenic chemicals in raising lowered blood prothrombin levels has been amply demonstrated. 2-methyl-1,4-naphthoquinone by the intravenous method of administration has proved highly effective. The minimum effective dose has been found to be 2 mg. for the adult. Although this dose has had a definite effect within two hours and has raised low levels to an entirely normal figure in twenty hours, it may well be that larger doses would result in earlier normal values and that the duration of effect might be substantially prolonged. Further investigation along these lines is to be desired. The possible prolongation of effect with greater doses depends largely on the ability of the body and especially of the liver to store prothrombin or its precursor, a point needing clarification.

Although severe liver damage appears necessary to prevent adequate elevation of the blood prothrombin after the intravenous injection of 2-methyl-1,4-naphthoquinone, lesser degrees of liver impairment appear to lead to a slower onset of response, a lessened height of response and a response of shorter duration. Under certain circumstances the application of these facts may be of definite value in determining the degree of impairment of one important liver function. We feel that transfusions should be delayed when possible until after the patient's response to the prothrombogenic substance has been determined in order that poor liver function

may not be obscured. Patients who have been unable to raise their prothrombin to a normal level when 2-methyl-1,4-naphthoquinone has been given intravenously before operation have done poorly after operation.

While the intravenous mode of administration presents definite advantages under circumstances in which oral administration is not feasible, as in nauseated patients or when the most rapid effect is essential as in bleeding, we do not propose that this route be used in all cases, the oral method being considered simpler for the average patient. The instability of the aqueous solution of 2-methyl-1,4-naphthoquinone and the ease with which this chemical is precipitated from solution when chilled are disadvantages to its routine use.

As previously stated, we have considered any prothrombin figure 90 per cent or above as normal. We wish to stress the importance of attaining an entirely normal figure before surgery is attempted, since it is wise to know that a normal level can be reached or that liver damage prevents this response. Much prothrombin may be lost during operation because of blood loss, and this may cause the already lowered prothrombin to fall to a dangerous level. We have found that in some cases bleeding may occur with a prothrombin level as high as 70 per cent of normal, although this is true usually for patients with considerable liver damage and confirms the probability that other factors are involved in this bleeding.

SUMMARY

1. 2-methyl-1,4-naphthoquinone has been administered intravenously to twenty-two patients. It has proved to be efficient in raising the prothrombin level. Bile salts were not necessary for this response.
2. With the exception of local distress of short duration at the time of injection, no toxic manifestations have been observed.
3. The minimal effective intravenous dose of 2-methyl-1,4-naphthoquinone in the adult was found to be 2 mg.
4. In cases uncomplicated by liver impairment a 2 mg. dose given intravenously raised the prothrombin level from 50 per cent to 80 per cent in an average of seven and one-half hours and to 100 per cent in an average of twenty hours.
5. A 2 mg. intravenous dose kept the prothrombin level above 90 per cent of normal for four or more days unless liver damage was present.
6. Severe liver damage permitted only a slight response to intravenous 2-methyl-1,4-naphthoquinone. If liver impairment was less marked, the effect was manifested in a slower onset of response, a lessened height of response, and a shorter duration of response.
7. Bleeding was rapidly and effectively controlled unless severe liver damage was present.
8. The intravenous route of administration has great value in patients for whom oral administration is difficult or impossible, as well as in those cases in which rapid cessation of bleeding is imperative.

A Pilot May Faint.—Human physiology sets no definite speed limit, but, if you are going fast, turning is dangerous, because it drains the blood into the parts of the body on the outside of the turn and may cause fainting. In particular, if a pilot turns a rapidly moving aeroplane upwards, his blood is forced down into his legs, and he may faint.—Haldane, J. B. S.: *Science and Everyday Life*, New York, Macmillan Company, 1940.

ORTHOSTATIC HYPOTENSION AND
ORTHOSTATIC TACHYCARDIA

TREATMENT WITH THE "HEAD-UP" BED

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Orthostatic hypotension is characterized chiefly by a sharp decrease in blood pressure when a patient afflicted with it stands. The blood pressure is ordinarily normal when the patient lies. If the blood pressure decreases to a low level, weakness and syncope result. Other relevant signs or symptoms are deficient sweating, either localized or generalized, secretion of larger amounts of urine when the patient is recumbent than when he is erect and in some cases a failure of the pulse rate to increase markedly when the patient assumes the erect posture. Orthostatic hypotension should be suspected whenever a patient has exhaustion in the morning which lessens during the day, whenever weakness, dimness of vision or syncope occurs on assumption of the erect posture and disappears on lying down, whenever episodes of syncope are inadequately explained and whenever there is diminished sweating. This condition has been considered by some to be the result of failure of adequate constriction of arterioles when patients stand.¹ The failure of the arterioles in turn has been assumed to result from a defect in the autonomic nervous system. This concept has been based on logical interpretations of clinical data: 1. Extensive sympathectomy in cases of essential hypertension results in a diminution of arteriolar tone which has seemed to explain the orthostatic hypotension which ordinarily results from extensive sympathectomy. 2. Drugs which increase arteriolar tone dramatically relieve the orthostatic symptoms and markedly improve the blood pressure in the erect posture.² The natural assumption followed that it is deficiency in arteriolar resistance which results in the low blood pressure when the patient stands. 3. The disturbances in sweating frequently found in cases of orthostatic hypotension have appeared to demonstrate a primary disturbance in the autonomic nervous system.¹ Hypofunction of this cholinergic part of the autonomic nervous system seemed an index of a similar disturbance in the adrenergic portion of the autonomic nervous system which resulted in a loss of arteriolar tone.

Recent studies, which we are not presenting in detail in this paper, suggest that the defect in postural adaptation is not a defect in arteriolar vasoconstriction but rather one in the maintenance of adequate return of venous blood to the heart. The evidence in brief may be summarized as follows: 1. Weiss and his associates have shown that circulatory collapse may be induced by the erect posture when normal subjects

are given appropriate amounts of sodium nitrite.³ Syncope produced by this artificial method appears to be the result of the loss of venous tone and the pooling of blood in the dependent portions of the body and closely resembles the syncope observed in cases of orthostatic hypotension. 2. We have been able to demonstrate a deficient "potential" in the venous return to the heart in all cases of orthostatic hypotension which we have studied by the Flack test, which consists in having the patient blow against the column of mercury of a sphygmomanometer with the glottis open.⁴ The resulting increase in intrathoracic pressure increases the resistance which the venous blood has to overcome in traveling back to the right side of the heart and is a measurement of the potential of the venous return. Normal subjects can maintain the mercury column at 40 mm. of mercury for periods of at least twenty-five seconds, with little change in pulse rate or blood pressure. Patients with orthostatic hypotension become pulseless and collapse within a period of ten seconds. Fluoroscopic and roentgenographic studies of the heart show a diminution in the size of the heart and great vessels during this period of increased intrathoracic pressure (fig. 1). However, when these patients are placed in a recumbent position with the head 30 degrees lower than the feet, the Flack test approaches normal in some cases. 3. The temperature of the skin of the toes and of the fingers of two individuals with orthostatic hypotension changed in a normal fashion in response to different environmental temperatures and to application of heat to the trunk. These studies indicate that the peripheral arterioles respond normally by dilatation and constriction in a reflex manner to changes in temperature. The autonomic innervation of the arterioles seemed, therefore, to be intact functionally.⁵ 4. In cases of orthostatic hypotension the peripheral arterioles offer adequate resistance to maintain the blood pressure at normal levels when the patient is recumbent. It seems illogical that simple assumption of the erect posture could cause loss of arteriolar tone. 5. The arteriolar vasoconstricting substances ephedrine, epinephrine, paredrinol (racemic parahydroxy- α ,N-dimethylphenethylamine) and amphetamine raise the whole level of blood pressure in cases of orthostatic hypotension, but use of them does not prevent the abnormal decrease in blood pressure when patients stand.

These five observations suggest that there is no deficiency in arteriolar tone in the syndrome of orthostatic hypotension but rather that there is a diminution in the maintenance of adequate return of venous blood to the heart, which results in a diminished cardiac output and a decrease in the arterial blood pressure when patients stand.

ORTHOSTATIC HYPOTENSION

An attempt to find a remedy for orthostatic hypotension in the field of vasoconstricting drugs has proved in our hands disappointing. We have used ephedrine,

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5. Fetherree, T. J., and Allen, E. V.: Sympathetic Vasodilator Fibers in the Upper and Lower Extremities: Observations Concerning the Mechanism of Indirect Vasodilatation Induced by Heat, *Arch. Int. Med.* 62: 1015-1028 (Dec.) 1938.

paredrine (parahydroxyphenylisopropylamine), prostigmine methylsulfate and guanidine hydrochloride. These substances have given symptomatic relief and they have prevented the reduction of blood pressure to a low level when patients stand. However, in two cases which we studied carefully the beneficial results were only temporary.

During investigation of the value of various therapeutic procedures, we noted that patients with orthostatic hypotension appeared to improve symptomatically and objectively during the daytime and that this improvement had disappeared in the morning after sleep in bed at night. The implication in this observation was that these patients lost some of their ability to adapt themselves to changes in posture as the result of either sleep itself or as a result of the recumbent position in which they slept. This observation led to the suggestion that patients with orthostatic hypotension should not sleep in a flat bed but should lie in a semi-inclined or "head-up" position⁶ (fig. 2). The results of this type of treatment have been so startling

resulted in improvement in the subjective symptoms. When the patient stood his blood pressure was higher than before the drug was given. Guanidine hydrochloride given orally was even more beneficial and on this medication he remained free from symptoms for a week. At the end of this time both prostigmine and guanidine appeared to lose their effect, and the patient reverted to his former condition. Medication with ephedrine and amphetamine was only temporarily beneficial. The patient's condition became steadily worse and for a period of three months prior to his last examination he was confined to bed and to a wheel chair.

The patient returned to the clinic March 25, 1940. The orthostatic hypotension had greatly increased. Several determinations of blood pressure with the patient recumbent averaged 130/80. The patient was unable to stand erect for longer than three minutes because of syncope which then occurred. The blood pressure at the end of one minute of standing in the erect posture could not be obtained. The patient was unable to sweat over the face, trunk and extremities when his body was subjected to radiant heat. Paredrinol, prostigmine methylsulfate, epinephrine and guanidine hydrochloride did not significantly change the blood pressure when the patient was erect or alleviate the patient's disability (fig. 3).

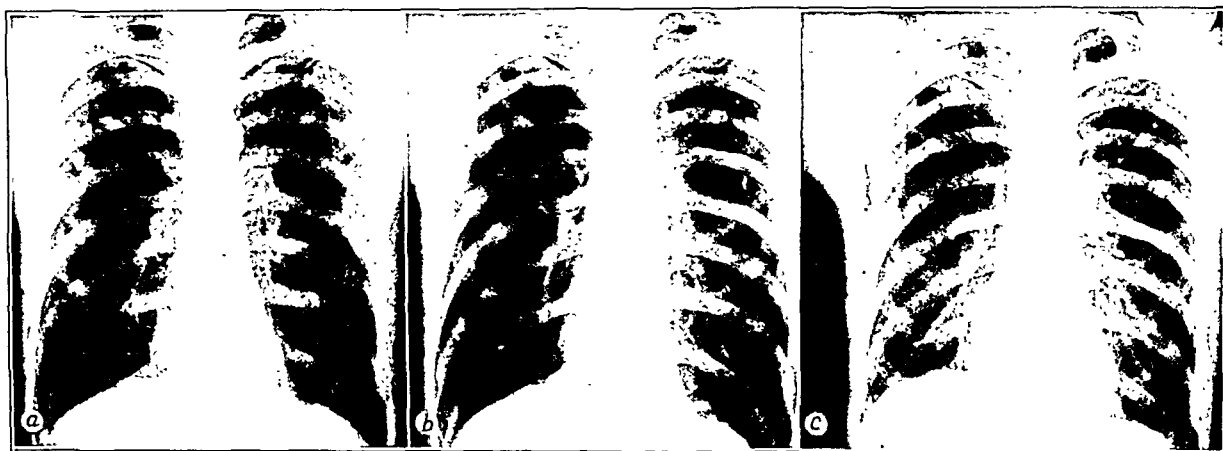


Fig. 1.—Evidence of the effect of increased intrathoracic pressure on size of the heart and great vessels: (a) control; normal inspiration; (b) Flack test of 40 mm. of mercury at the end of five seconds; (c) expiration at the completion of the Flack test.

that we are reporting illustrative cases. The following is a case of spontaneous orthostatic hypotension:

A man aged 59 first registered at the Mayo Clinic July 5, 1939. He complained of dizziness, blurring of vision, exhaustion and syncope associated with standing erect. These symptoms had begun insidiously a year prior to registration and had progressed to the point of severe disability. He was unable to walk more than two blocks without resting. He presented the typical features of spontaneous orthostatic hypotension. The recumbent blood pressure in millimeters of mercury was 130 systolic and 80 diastolic; at the end of one minute of standing it was 70/40. At the end of five minutes of standing the blood pressure was 55/45. The heart rate did not increase when the patient stood. The Flack test gave positive results. When the patient blew the mercury column to the 40 mm. mark, syncope resulted at the end of five seconds. When the patient was in the recumbent position and was tilted with the head down at an angle of 30 degrees, he was able to blow the mercury column to the 50 mm. mark and retain it there for a period of twenty-two seconds without syncope. Roentgenoscopic and roentgenologic studies of the heart during the periods of increased intrathoracic pressure showed diminution in the size of the heart and in the size of the great vessels in the mediastinum when the patient blew against a column of mercury. The administration of prostigmine methylsulfate subcutaneously

The patient was then placed in a bed the head of which was elevated 18 inches. During the daytime he was encouraged to sit in a chair. Improvement occurred quickly. The patient was able to stand erect for longer and longer periods. He became more active and was capable of walking for short distances. At the end of four days of this treatment the patient was able to stand erect for periods longer than an hour without syncope. When he stood the blood pressure slowly fell from 100/60 to 60/40 at the end of an hour (fig. 4). Previously the best effect of treatment was ability to stand ten minutes following the injection of epinephrine (fig. 3). The improvement could be made to disappear, for when the patient slept one night in a level bed the blood pressure on the following morning when he was in the erect posture could not be obtained and syncope occurred within one minute.

The patient has continued to sleep on the tilted bed since that time. Within two weeks he went to work for the first time in seven months. Two months after treatment on the tilted bed had been begun he had not had an attack of syncope. At present he works six hours a day in his office and two hours a day in his garden. He has recovered his ability to sweat over his face, arms and trunk. He is not, however, cured of vascular disability, for he still has orthostatic hypotension. In the erect posture the blood pressure still decreases to 60/40 at the end of an hour, but he has recovered a measure of postural vascular adaptability sufficient to allow him to function in a comparatively normal fashion. We do not pretend that the tilted "head-up" bed alone has been responsible for this improvement. It has been instrumental in preventing the loss of postural

⁶ Paper to designate a bed with the head of the head of a bed on 18 inches. Patients sleep comfortably in this position, although some may need a hard pillow under the mattress at the level of the thighs to prevent slipping.

vascular adaptability which the patient gained during the day-time and which previously he had been losing by sleeping on a flat bed.

The following case is one of orthostatic hypotension induced by sympathectomy for essential hypertension:

A woman aged 34 had an extensive sympathectomy performed May 28, 1940, because of essential hypertension. June 6 a similar operation was performed on the left side. June 24 the blood pressure decreased from 160/110 when she lay to 60/40 after standing for forty-five seconds, at which time she became so weak that she was forced to lie again to prevent syncope. The pulse rate increased from 94 per minute on lying to 140 when she stood. For three days she slept on the "head-up" bed at night and sat in a chair or walked a little during the day. At the end of this period she could stand or walk without weakness or syncope. She felt entirely well and she was able to stand for thirty minutes without symptoms. The blood pressure when lying was 130/100 and her pulse rate 70 per minute. The blood pressure when she stood was 150/100 and the pulse rate was 100. For the next twenty-four hours the patient slept on a horizontal bed at night and continued as active as her strength permitted during the day. The blood pressure while lying in bed then was 144/110 and the pulse rate 78. She could stand for only forty-five seconds because of weakness. The systolic blood pressure at the end of this time was 50 mm. of mercury and the diastolic blood pressure could not be determined. The pulse rate was 130 per minute. During the next

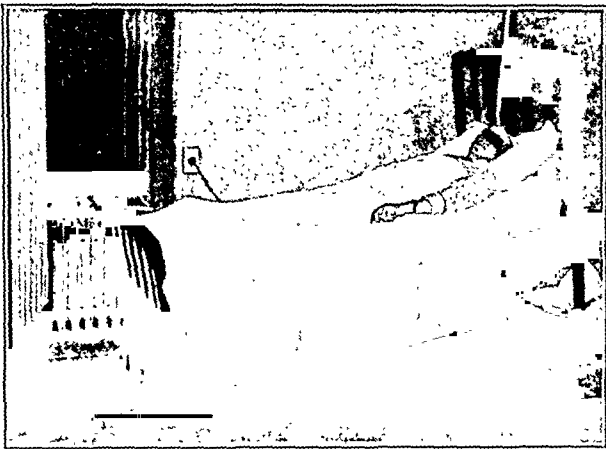


Fig. 2.—The tilted "head-up" bed.

day she rested or slept on the "head-up" bed or rested in a chair. At the end of this period when she lay in bed the patient's blood pressure was 148/112 and her pulse rate was 90. At the end of five minutes of standing the blood pressure was 96/70 and the pulse rate 138. She felt better than she had on the day before but did not feel entirely well. The patient continued to sleep or rest on the "head-up" bed for two days and her condition continued to improve. At the end of this time, the respective values for blood pressure and pulse when she lay were 140/112 and 72. After five minutes of standing they were 146/110 and 124. She felt entirely well. During a subsequent period of twenty-four hours she slept or rested on a horizontal bed. At the end of this time she was unable to stand for a minute because of syncope. The blood pressure was indiscernible and the pulse rate increased to 150 per minute just before she fainted.

Study of the patient demonstrated unequivocally that resting and sleeping on the "head-up" bed prevented orthostatic hypotension and the symptoms associated with it.

ORTHOSTATIC TACHYCARDIA

We have given the name orthostatic tachycardia to a syndrome which is characterized by an excessive acceleration of the heart when the patients change from the recumbent to the erect posture. Orthostatic exhaustion, blurring of vision, weakness on exercise and syncopal episodes may occur. There is usually no

orthostatic hypotension present. Sweating is normal. This is a syndrome which seems identical with or similar to those characterized as effort syndrome, irritable heart or neurocirculatory asthenia. The symptoms and objective signs are immediately relieved when the patients lie down and as with orthostatic hypotension these patients exhibit an exacerbation of symptoms in the morning following a night of rest on a flat bed.

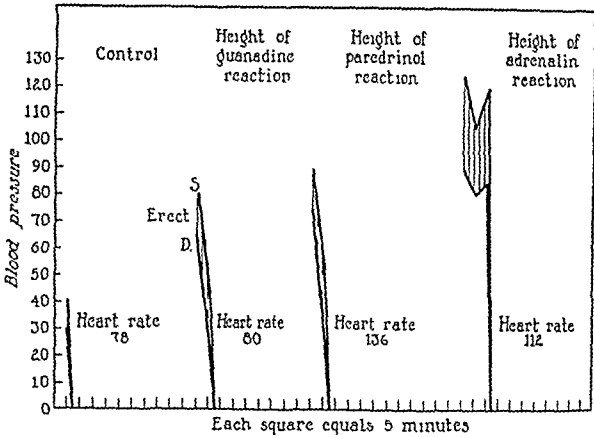


Fig. 3.—Blood pressure determinations in the erect posture following 0.75 Gm. of guanidine hydrochloride administered orally, 40 mg. of paredrinol sulfate administered intramuscularly and 1 mg. of epinephrine administered subcutaneously. In each instance the upper line indicates the systolic blood pressure and the lower line indicates the diastolic blood pressure. They are designated S and D respectively in that part of the chart showing the effect of guanidine. During the control period the patient fell in syncope at the end of one minute. At the height of the reactions to guanidine and paredrinol the patient fell at the end of five minutes. At the height of the reaction to epinephrine the patient fell at the end of ten minutes.

Symptoms and objective signs improve during the course of the day.

In our experience the Flack test has demonstrated an inherent defect in the mechanism for returning venous blood to the heart similar to that demonstrated in cases of orthostatic hypotension and it is our impression that the underlying pathogenesis is a diminution of "potential" of return of venous blood to the heart

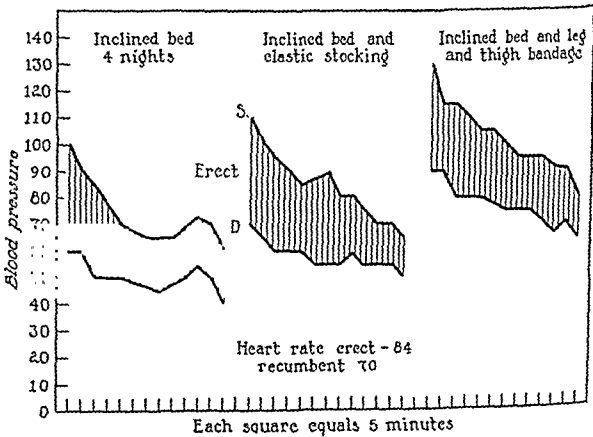


Fig. 4.—Blood pressure determinations in the erect posture after four nights of treatment with the tilted "head-up" bed. The patient was capable of standing for an hour without syncope.

rather than defective arterioles. It would appear that if these patients did not have orthostatic tachycardia they might have orthostatic hypotension. Following is an illustrative case of orthostatic tachycardia:

A physician aged 30 registered at the Mayo Clinic May 15, 1940. He complained of exhaustion and attacks of unconsciousness. Symptoms had begun a year and a half previous to registration, when he was working for long hours in a hospital spending many nights sitting up with his father, who was very

ill. At that time his wife noticed episodes characterized by unsteadiness in standing and walking, slowness and uncertainty of speech and pallor and exhaustion. His condition became progressively worse. The patient omitted breakfast once in September 1939 and an hour after arising fell and was unconscious for a minute. Hypoglycemia was suspected but studies of sugar in the blood did not confirm this suspicion. The exhaustion, weakness and difficulty in talking and walking became more pronounced, forcing the patient to terminate his hospital appointment and to go into general practice. In May 1940 he experienced two more episodes of unconsciousness of short duration.

A general physical examination demonstrated no abnormalities of note. A repetition of the dextrose tolerance studies and a thirty hour fast appeared to exclude hypoglycemia as a cause for the patient's ill health. Neurologic and electro-encephalographic examinations gave essentially negative results. The patient, however, had marked orthostatic tachycardia. In the recumbent position the blood pressure was 155/90, with a heart rate of 80 per minute. When in the erect posture the blood pressure varied between 120/80 and 100/70 and the heart rate averaged 150 beats per minute. The Flack test demonstrated a marked deficiency in the potential of venous return. When the patient blew the mercury column to the 40 mm. mark, the pulse disappeared at the end of ten seconds and the patient experienced a marked feeling of weakness and syncope.

In view of the obvious orthostatic vascular defects, the patient was questioned in detail concerning the time his symptoms occurred and it was discovered that the exhaustion, weakness and syncope episodes had all occurred during the morning hours shortly after arising from a night of rest in bed. The patient and his wife had noticed that he improved as the day progressed unless he was subjected to some unusual strain.

The patient was placed on a tilted "head-up" bed, the head of which was raised 18 inches. On the following morning a distinct improvement occurred subjectively and this improvement was reflected in the heart rate with the patient standing. Following the second night on the tilted bed the patient's blood pressure in the erect position was 130/90, with a pulse rate of 80 beats per minute. This improvement continued as long as the patient was kept on the tilted bed at night. When he was again placed on a flat bed he reverted overnight to his previous condition, associated with a heart rate of 140 beats per minute when standing.

The patient returned home on a regimen of increased physical exercise and of sleeping on a tilted bed at night. His pulse rates in the erect posture and after mild exercise consistently remained less than 100 beats per minute. He experienced a return to normal health. One month after returning home, the patient was asked to sleep on a flat bed and within forty-eight hours his symptoms of exhaustion and weakness had returned and he experienced a severe syncope episode with loss of consciousness. He promptly returned to the use of a tilted bed and all symptoms completely disappeared within twenty-four hours. He has written: "My work has been very heavy during the past weeks but I have been able to do it with far greater ease than ever before. After returning to the tilted bed there have been no periods of weakness or any other symptoms."

The following case is illustrative of a combination of orthostatic hypotension and tachycardia associated with the clinical picture of subacute combined sclerosis:

A woman aged 47, who registered at the Mayo Clinic June 10, 1940, complained of numbness and tingling of the finger tips, weakness and staggering gait of six months' duration. She had had anemia for twenty years and recurring attacks of glossitis for ten years. Achlorhydria was known to have been present for eight years. She had been treated with iron but not with liver.

The average number of erythrocytes was 3,300,000 per cubic millimeter of blood. The concentration of hemoglobin was 8.5 Gm. in each 100 cc. of blood and the color index was less than 1. Hypochromic anemia was apparent on microscopic examination. The majority of the erythrocytes were microcytes but there was an occasional macrocyte. There was no shift of the polymorphonuclear leukocytes to the right. Free hydrochloric acid was absent in the gastric contents, even after stimulation with

histamine. Neurologic examination demonstrated the typical symptoms and signs of subacute combined sclerosis consisting of marked diminution of the deep reflexes of the lower extremities, bilateral Babinski phenomena, ataxic gait and absent vibration sense over the lower extremities and iliac crests. Joint sense of the legs was markedly impaired and Romberg's sign was present. During the process of the neurologic examination the patient fainted and examination of blood pressure in the recumbent and erect postures revealed the existence of orthostatic hypotension.

In the recumbent position the blood pressure averaged 160/110, a heart rate of 84. In the erect posture at the end of one minute of standing the blood pressure was 60/50, with a heart rate of 140. The patient was unable to stand for periods longer than three minutes without falling as a result of syncope. The Flack test gave markedly positive results. Detailed vascular examinations were conducted over a period of three days and very severe orthostatic tachycardia and hypotension of the degree already noted were found on every occasion. During this period of control the hematocrit estimation was 36 and studies of blood volume conducted by means of the congo red method demonstrated a total volume of 2,585 cc. of plasma or 45 cc. per kilogram of body weight. The total volume of whole blood was 4,038 cc. or 70 cc. per kilogram of body weight.

The patient was then placed on the tilted "head-up" bed with the head of the bed elevated 18 inches. The patient was encouraged to sit in a chair for as long as possible during the daytime and was forbidden to lie on a flat bed. During the course of three days no change could be detected in symptoms or in the signs of tachycardia or hypotension. On the fourth day, coincidental with the appearance of slight edema of the lower extremities, the clinical picture changed dramatically. In the recumbent position the blood pressure was 164/94, with a pulse rate of 80. With the patient in the erect posture, at the end of one minute the blood pressure was 166/98, with a heart rate of 96. At the end of ten minutes of continuous standing the blood pressure was 138/92, with a heart rate of 104. At the end of a half hour of continuous standing the blood pressure was 120/80, with a heart rate of 116. The patient was able to walk alone without assistance for the first time since admission to the hospital.

She was then placed on a flat bed for ten minutes, and studies of blood volume were conducted. The hematocrit index was 34. The total volume of plasma was 2,930 cc. or 51 cc. per kilogram of body weight. The total volume of whole blood was 4,448 cc. or 78 cc. per kilogram of body weight. There had been an apparent increase of 410 cc. in the volume of whole blood. Immediately after the determinations of blood volume were made, the patient was again placed on the tilted bed regimen. The improvement in symptoms, heart rate and blood pressure with the patient in the erect position was maintained.

In view of the fact that the patient had received three injections of liver parenterally at the time of her first admission to the hospital, the improvement could not be ascribed alone to the tilted bed. To evaluate the effect of the tilted bed the patient was placed on a flat bed for forty-eight hours. During the first twenty-four hours no appreciable change could be noted in the heart rate or blood pressure with the patient in the erect posture. At the end of forty-eight hours coinciding with the disappearance of the slight edema of the lower extremities the patient reverted to her previous condition. She was unable to stand for periods longer than a minute without syncope. The blood pressure with the patient recumbent was 140/80, with a heart rate of 80 beats per minute. Blood pressure in the erect posture at the end of half a minute was 60/45, with a heart rate of 130. The patient was again placed on the tilted "head-up" regimen and within forty-eight hours had completely regained postural vascular adaptability and was able to walk without assistance. During the course of three weeks of observation in the hospital she has remained on the tilted bed regimen and has not had a syncope episode. The blood pressure and heart rate have remained consistently normal when she stands. With her increased ability to exercise, the edema of the lower extremities has disappeared. The signs of subacute combined sclerosis are still present. In spite of extensive liver parenterally administered the patient's blood picture has remained unchanged. The concentration of hemo-

globin is 8.1 Gm. per hundred cubic centimeters of blood. The erythrocytes number 4,100,000 per cubic millimeter of blood. Examination of the blood smear reveals hypochromic microcytic anemia with an occasional macrocyte.

An interesting feature of this case is the patient's history of twenty years of exhaustion and syncopal episodes. Every morning in these twenty years she had experienced severe exhaustion and dizziness during the first two hours after arising from bed. She had warned her class in school not to be concerned if they saw her put her head on her desk to keep from fainting. For twenty years she had not dared to kneel or stand in church for fear of fainting. During the afternoons and evenings of these twenty years the exhaustion would disappear and her tendency to faint would vanish, only to reappear again the following morning, after a night's rest in bed. Since institution of the tilted bed regimen the morning exhaustion, faintness and tendency toward syncope have disappeared in spite of the presence of subacute combined sclerosis. This patient was observed six months later. She had been treated persistently with liver extract and had slept on the "head-up" bed. The anemia and symptoms of subacute combined sclerosis were greatly improved. Orthostatic hypotension was absent but she stated that when she slept on a flat bed symptoms of this condition recurred.

COMMENT

It appears that there is an inherent defect in the ability to return venous blood to the heart when patients stand, in the syndromes of primary orthostatic hypotension and orthostatic tachycardia as well as in cases of secondary orthostatic hypotension following extensive sympathectomy for essential hypertension. This defect in the "potential" of venous return can be demonstrated objectively by means of the Flack test.

The tilted "head-up" bed has improved significantly the ability of the circulation of these patients who have orthostatic hypotension and orthostatic tachycardia to adapt itself to the erect posture as shown by objective study of the cardiac rates and blood pressures in the erect posture. These studies have corroborated the marked subjective improvement which follows this type of therapy. The improvement is maintained if use of the tilted bed at night is continued. Rest on the ordinary flat bed for a night or for several nights is sufficient to cause a reversal of the patient's condition and reestablish the original pattern of vascular maladaptation characterized by orthostatic tachycardia and hypotension and by recurrence of symptoms. Some patients with orthostatic tachycardia and orthostatic hypotension are not benefited by this type of treatment. The reasons are obscure.

It appears that rest and sleep on the tilted bed have prevented loss of that measure of postural adaptation which the patient himself has gained during the daytime, by some physiologic process attendant on increased activity in the erect posture. Whether this gain results from readjustments of activity of the autonomic nervous system to the muscles in the walls of the veins, whether there is a change in the tone of striated muscle, an increase in the content of extracellular fluid in the extremity, an increase in the volume of circulating blood or an intrinsic increase in venous or capillary tone is at the present time impossible to say. Investigation now being conducted suggests that the improvement in postural vascular adaptability coincides with an increase in the volume of circulating blood and a definite increase in the content of extracellular fluid in the lower extremities. It would seem logical to assume that the increased pressure of extracellular fluid would prevent in some degree pooling of blood in the legs with the patient in the upright position. We make the tentative suggestion that the content of extracellular fluid in the lower extremities

is increased by the "head-up" posture and prevents pooling of venous blood in the legs as a result of increased tissue pressure. Return of venous blood to the heart is thus maintained in a fashion approaching normal. Studies are being conducted at the present time to determine the value of the "head-up" bed in cases of hypertensive headache, nocturnal epilepsy, exhaustion syndromes during convalescence and other disabilities that are associated with definite postural features.⁷

CONCLUSIONS

Elevation of the head of the bed for some patients with orthostatic tachycardia and for some patients with orthostatic hypotension prevents acceleration of the pulse rate and decrease in blood pressure when such patients stand. There is a coincidental improvement in symptoms. The "head-up" bed is in our experience the most satisfactory method of treatment for orthostatic tachycardia and orthostatic hypotension.

ABSTRACT OF DISCUSSION

DR. HORACE M. KORN, Iowa City: The idea that the cause of orthostatic hypotension is to be sought in a disturbance of the mechanisms which normally provide, under all conditions, an adequate flow of blood from the veins to the heart is new, as far as I know, and is certainly attractive. Furthermore, it seems to me that likening the mechanism to that of nitrite shock is quite reasonable. Although, naturally, a larger series of cases will have to be collected before final conclusions can be drawn, the results obtained in these two cases by having the patient sleep with his head slightly elevated, which, theoretically, would tend to increase venous tone, strongly suggest that the authors' conception of the pathologic physiology of orthostatic hypotension is correct. I cannot help feeling, however, that hypotension alone is not the sole cause of the symptoms in this disease. After long observation of a typical case, Dr. W. L. Randall and I came to the conclusion that maintaining the blood pressure at an essentially normal level, which we were able to do by means of parendrine, was not enough in itself to relieve the patient of the lassitude and fatigability which are so characteristic. Only when, in addition, we produced psychic stimulation by giving amphetamine sulfate were the subjective manifestations dispelled. Patients with orthostatic hypotension may be subject to spontaneous hypoglycemia, as our patient was, and, if this complication is not recognized whenever it occurs, our efforts to evaluate any form of therapy may be confounded.

DR. O. P. J. FALK, St. Louis: The authors' significant observations are so definite and clearcut that they need little comment. This syndrome has had little light cast on it since the original observations of Bradbury and Eggleston in 1925. My interest in this syndrome was stimulated by observations on some sympathectomized hypertensive subjects on whom the usual phenomena of postural hypertension were observed. It seemed that there were a good many people who had not been sympathectomized but who had somewhat similar symptoms, and on checking postural blood pressure observations on them I was able to confirm the fact that there were a good many subclinical cases of postural hypotension going about unrecognized. I, like Drs. MacLean and Allen, have observed that these people respond to some of the drugs that they have mentioned, including amphetamine sulfate, neosynephrin and parendrine, but not to any permanent or sustained degree. Parendrine (20 mg. once or twice daily) seems to have the most marked and best sustained pressor effect. I wish to make a plea for a little more careful observation on some of these people who complain of such symptoms as undue fatigability and weakness or unsteadiness on standing, by checking their blood pressures in the stand-

7. Since this paper was written five additional patients with orthostatic hypotension and nineteen patients with orthostatic tachycardia have been treated on the "head-up" bed. Marked reversible improvement resulted in four of the cases of orthostatic hypotension and in sixteen of the cases of orthostatic tachycardia. Ten patients with chronic daily morning headaches have been studied. Six of these patients have obtained specific relief from pain in the head by the use of the "head-up" bed at night.

ing as well as the sitting and lying positions, so that these subclinical types will be recognized.

DR. A. R. MACLEAN, Rochester, Minn.: Several of our patients with orthostatic tachycardia have given histories suggestive of hypoglycemic episodes. Fasting blood sugar estimations, sugar tolerance curves and prolonged periods of fasting have definitely ruled out any primary hypoglycemic pathogenesis. However, blood sugar estimations in the lower range of normal values are not uncommon among individuals with tachycardia in the erect posture. This tendency may represent another phase in the disturbed physiology which results in a diminution of the venous return "potential." I wish to emphasize two important features of our work. We have very definite clinical proof that the "head-up" bed has accomplished a return of a large portion of postural vascular adaptability in patients with orthostatic hypotension and tachycardia. It has not cured them. We do not know how this improvement has been brought about. Some of our cases show an actual increase in the circulating blood volume following therapy. All of our cases appear to have an increase in the extracellular fluid content of the lower extremities. We can only say that the use of the head-up bed appears to have accomplished a relative increase in the circulating blood volume as compared to the total cross section of the vascular bed.

Clinical Notes, Suggestions and New Instruments

SUCCESSFUL SUBLINGUAL THERAPY IN ADDISON'S DISEASE

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SAN FRANCISCO

AND
EDWARD HENDERSON, M.D.
BLOOMFIELD, N. J.

Desoxycorticosterone acetate has been found highly effective in the treatment of Addison's disease. It is generally given in oil by subcutaneous or intramuscular injection but is being employed also in the form of pellets implanted under the skin. The latter method of administration is a precarious one, since there is no way of controlling dosage; excessive absorption of the active principle from pellets, as manifested by edema and anasarca, elevation of blood pressure to hypertensive heights and occasionally fatal circulatory collapse, has been reported by Loeb¹ and others. Subcutaneous and intramuscular injections, on the other hand, allow control of the dose administered, but they are often a source of great inconvenience and no little expense.

The ingestion of tablets of desoxycorticosterone acetate is for practical purposes valueless. Two of our patients with Addison's disease who ingested ten times the dose of desoxycorticosterone acetate effective by the subcutaneous route developed symptoms of adrenal cortical insufficiency. Kuizenga, Nelson and Cartland² have shown in experiments on the rat that this substance is less than one thirty-fifth as effective orally as parenterally.

In connection with this problem of an effective oral form of desoxycorticosterone acetate which would be rapidly absorbed, it was concluded that, since the ranine veins and ranine artery—besides the mass of capillaries and available lymphatics—are so near the surface and so exposed as to be more readily available for absorption of a substance when applied topically

than any other part of the body, sublingual administration of steroids in solution appeared to be entirely practicable.

It was found that desoxycorticosterone acetate dissolved in propylene glycol administered by drops under the tongue was as effective in the cases herein reported as when given in oil subcutaneously or intramuscularly. Each cubic centimeter of propylene glycol contained 10 mg. of desoxycorticosterone acetate. The dropper used by the patients was such that 1 cc. of the solution was discharged as 40 drops. Hence 4 drops contained 1 mg. of desoxycorticosterone acetate. The dose was adjusted to the needs of the patient, from 8 to 24 drops of the solution, or 2 to 6 mg. of the active substance, being given daily in divided doses.

All six patients who have been receiving desoxycorticosterone acetate sublingually for from six to eight weeks are in excellent condition and are carrying on their usual occupations. A brief report of the status of these patients follows:

REPORT OF CASES

CASE 1.—H. E. L., a man aged 29, had had the characteristic signs and symptoms of Addison's disease since 1936. His usual weight of 135 pounds (61 Kg.) had fallen to 112 pounds (51 Kg.). A diffuse bronze pigmentation of the skin and of the buccal and pharyngeal mucous membranes was noted. Blood pressure ranged from 90 systolic, 40 diastolic to 100 systolic, 60 diastolic. Roentgenograms in 1936 failed to reveal any changes in the adrenals and lungs.

From April 1937 to September 1939 the patient was treated with various preparations of adrenal cortex extract. For about a year thereafter he received desoxycorticosterone acetate from 2.5 to 5 mg. intramuscularly once daily. By Aug. 22, 1940, his weight had increased to 123 pounds (56 Kg.), his blood pressure was 95 systolic, 60 diastolic and he felt well but, as during the past four years, he was unable to carry on his occupation. At that time sublingual administration of desoxycorticosterone acetate in propylene glycol was started, 4 drops being given five times a day (or 5 mg. of desoxycorticosterone acetate). He was instructed to take a well balanced diet and to discontinue the use of additional salt. When last seen, October 12, the patient weighed 127½ pounds (58 Kg.), his blood pressure was 95 systolic, 80 diastolic, and for the first time in four years he was carrying on his occupation as a ship inspector.

CASE 2.—M. L. M., a man aged 23, entered the hospital on June 18, 1940, his chief complaints being lassitude and extreme fatigability. Within a year his weight had fallen from 185 to 152 pounds (84 to 69 Kg.). A craving for salt had developed during the preceding three months. His blood pressure was 80 systolic, 60 diastolic and his skin showed deep pigmentation. Roentgenograms disclosed no abnormalities in the adrenal regions or the lungs.

Marked subjective improvement followed the administration of 10 mg. of desoxycorticosterone acetate once daily. His blood pressure had increased by July 16 to 110 systolic, 60 diastolic. Because of the development of edema at this time the dose of desoxycorticosterone acetate was decreased to 5 mg. a day. After the disappearance of edema the patient weighed 158 pounds (71.7 Kg.). Sublingual administration of desoxycorticosterone acetate in propylene glycol was started on August 27, the daily dose being 24 drops of the solution (containing 6 mg. of desoxycorticosterone acetate); at that time his blood pressure was 102 systolic, 60 diastolic and his weight 159½ pounds (72.3 Kg.). When the patient was last seen, October 10, he felt exceedingly well despite working long shifts as a taxicab driver. His weight was 165 pounds (75 Kg.) and his blood pressure 118 systolic, 80 diastolic.

CASE 3.—Baby R. M. (patient of Dr. H. E. Thelander), a boy born on Nov. 18, 1939, had symptoms of adrenal insufficiency dating from the time of his birth. The umbilical cord had been thrice encircled about the neck; cyanosis was marked and remained so for three days. On the eighth day after birth the baby vomited and had diarrhea. He responded well to the subcutaneous injection of salt solution and intravenous dextrose.

From the age of 5 weeks the baby received daily 1 mg. of desoxycorticosterone acetate by injection as well as adrenal cortex extract by mouth. His formula was made up with physiologic solution of sodium chloride. Temporary discon-

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The desoxycorticosterone acetate was supplied by the Schering Corporation for this study. The propylene glycol solution was made in our own laboratory. The crystalline material was added to the propylene glycol, which contained 10 per cent by volume of ethyl alcohol, and the material brought into solution by gentle warming. The alcohol was used to increase the solubility of the desoxycorticosterone acetate.

1. Loeb, R. F.: Adrenal Insufficiency, *Bull. New York Acad. Med.* 16: 347-367 (June) 1940.

2. Kuizenga, M. H.; Nelson, J. W., and Cartland, G. F.: Comparative Parenteral and Oral Assays of Adrenal Cortical Hormone Substances, *Am. J. Physiol.* 130: 298-303 (Aug.) 1940.

tinuance of the endocrine therapy was followed swiftly by signs of impending collapse. At the end of nine months the baby had gained well and reacted normally. On Aug. 25, 1940, sublingual use of desoxycorticosterone acetate in propylene glycol was begun, the dose being 2 drops five times a day (daily total of the substance, 2.5 mg.). After about seven weeks on sublingual therapy the baby is "strong and husky."

CASE 4.—D. J. W., a man aged 60, was admitted to the hospital on Aug. 19, 1940, in a state of collapse. He had had attacks of nausea and vomiting and pains in the abdomen for a period of two weeks. Considerable weight had been lost. His skin was deeply pigmented. The systolic blood pressure measured 90; the diastolic pressure could not be ascertained. Roentgenograms disclosed several rounded calcified foci in the lungs but no evidence of a change in the adrenals. The response to desoxycorticosterone acetate injected intramuscularly was highly satisfactory. At the time of discharge from the hospital, on September 5, the patient was receiving 5 mg. of desoxycorticosterone acetate daily.

When sublingual administration of desoxycorticosterone acetate in propylene glycol was begun on September 8 the patient felt well, his blood pressure was 115 systolic, 80 diastolic and his weight was 162 pounds (73.5 Kg.). The daily dose of the solution was 20 drops (or 5 mg. of the substance). On October 10 the patient stated that he felt very well and was fully able to carry on his occupation as a teacher. His blood pressure was 138 systolic, 80 diastolic and his weight 167 pounds (75.7 Kg.).

CASE 5.—S. K. (patient of Drs. Blair Holcomb, E. M. Burns and Hans Lisser), a man aged 35, since July 1937 had had attacks of nausea, vomiting and diarrhea which passed for "intestinal influenza." Following such an attack in 1938 the patient lost 30 pounds (13.6 Kg.) within a month. In July 1939, when seen by Drs. Holcomb and Burns, the patient presented a careworn and exhausted appearance, his skin was moderately pigmented, his blood pressure was 116 systolic, 80 diastolic, and he weighed 154 pounds (70 Kg.). He was given adrenal cortex extract subcutaneously and abundant salt by mouth. From Aug. 28 until Sept. 5, 1940, while under Dr. Lisser's care, the patient received desoxycorticosterone acetate intramuscularly 5 mg. a day and salt by mouth. He improved subjectively and his blood pressure rose to 140 systolic, 110 diastolic.

Since September 5 the patient has been taking desoxycorticosterone acetate in propylene glycol sublingually, 4 drops of the solution five times a day (a total daily dose of 5 mg. of the substance). On October 15 he weighed 152 pounds (69 Kg.), his blood pressure was 120 systolic, 86 diastolic, he appeared to be somewhat less pigmented and he stated that he felt better generally.

CASE 6.—Mrs. M. S. (patient of Dr. Helen Lee), aged 38, had had tuberculous peritonitis in 1927. In May 1938 she experienced a feeling of great fatigue and at about the same time noted that her skin was becoming pigmented. By April 1939 the tendency to fatigue had become more marked and there were occasional bouts of diarrhea. Roentgenograms disclosed a small calcified body overlying the upper pole of the left kidney. The blood pressure was 90 systolic, 50 diastolic and she weighed 131 pounds (59.4 Kg.). Impending collapse was prevented by the administration of adrenal cortex extract together with sodium chloride and sodium citrate. Since then she had taken adrenal cortex extract by mouth and by injection, together with large amounts of sodium chloride.

On Aug. 19, 1940, the sublingual use of desoxycorticosterone acetate in propylene glycol was begun. As in the other instances herein reported, the patient was instructed not to take salt in excess of that of the normal diet. At first 24 drops of the solution (6 mg. of the active substance) was given sublingually each day, but later, because of the development of edema about the ankles, the daily dose was reduced to 20 and later to 16 drops. The patient stated on October 19 that she felt considerably better on this regimen than she had heretofore and that she could now carry on her household and social activities without undue effort. On that day she weighed 140 pounds (63.5 Kg.) and had a blood pressure of 110 systolic, 80 diastolic.

SUMMARY

Desoxycorticosterone acetate dissolved in propylene glycol and administered by drops under the tongue has been found to be an effective form of replacement therapy in Addison's disease. The desoxycorticosterone acetate so administered seems to be as effective as that given in oil subcutaneously or intramuscularly.

Studies are now in progress as to the absorption of various endocrine substances when administered sublingually, particularly androgens and estrogens.

CHERRY STEM IN COMMON DUCT STONE

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LOS ANGELES

Foreign bodies are rarely considered a nucleus for stones found in the biliary tract. When encountered, however, they do present some interesting speculations.

REPORT OF CASE

A Negro youth aged 20, a student, admitted to the Los Angeles General Hospital Feb. 26, 1940, had been ill for ten days with nausea, vomiting and a sharp pain in the right upper quadrant of the abdomen. On the fifth day it was noted that he had acholic stools and also that he was jaundiced. He had a fever at times but no chills. There had been no antedating history of food intolerance or of similar attacks.

He was well developed and well nourished and in no great pain. The skin and scleras were jaundiced. There was rigidity in the right upper quadrant of the abdomen. Physical examination otherwise was negative. The hemoglobin content was 108 per cent, the erythrocyte count was 4,650,000 and the leukocyte count 13,400, with 83 per cent neutrophils, 3 per cent monocytes and 10 per cent lymphocytes. The urine gave a positive reaction for bile. The icteric index was 73. A flat x-ray plate of the abdomen was negative. His condition improved rapidly and he was discharged from the hospital March 7, only to return two days later with a recurrence of the same symptoms. He was again treated symptomatically and the condition rapidly cleared up again. March 21, a gallbladder dye study was made. There was no definite dye concentration: radiopaque calculi were not noted. He was discharged March 25. He felt well except for varying degrees of pain in the right upper quadrant and a poor appetite until May 22, when the pain again became severe and he reentered the hospital the following day.

His temperature was 103 F. and the blood pressure 105 systolic, 75 diastolic. He was in great pain, his face was flushed and the scleras were mildly icteric. There was rigidity of the right upper quadrant of the abdomen and the liver was palpable three fingerbreadths below the costal margin. The erythrocyte count was 4,500,000 and leukocyte count 13,100, with 86 per cent neutrophils. The icteric index was 40 on May 27 and 67 on May 30. He had an afternoon temperature of from 101 to 102 F. and stools were light yellow to gray until June 5, when he again became afebrile and asymptomatic.

At this time it was felt that an exploration should be done. Preoperative laboratory examination showed a cholesterol level of 208 mg. per hundred cubic centimeters of blood, a normal prothrombin content and an icteric index of 20, and oral cholecystography again showed no dye concentration.

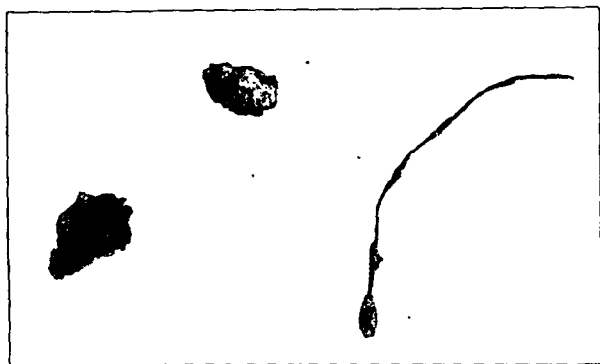
July 1 a laparotomy was performed (by a preceding service). The gallbladder was reported as "only slightly thickened and almost normal in appearance" by the surgeon but found to contain very small flaky stones. The common duct was opened and some of the same material found. A catheter was placed in the common duct and the gallbladder removed. He made an uneventful recovery and on July 9 a cholangiogram revealed moderate dilatation of the intrahepatic ducts. There was a smooth 1.5 cm. ovoid shadow in the distal end of the common duct about which a small amount of dye could be forced. These conditions were consistent with an impacted stone at the distal end of the common bile duct. Several methods of flushing the

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duct, after attempted fragmentation of the stone with ether, were attempted. Atropine, glyceryl trinitrate, desoxycholic acid and magnesium sulfate were of no avail, as the shadow persisted. The prothrombin time was checked and found normal.

July 29 exploration was done (by C. J. B.). The common duct was fixed in edematous adhesions from the previous operative procedure. It was explored but only flakes of stony material were obtained. The retroduodenal portion was then explored by mobilization of the duodenum according to the method of Kocher. The common duct was noted to traverse intrapancreatically and in that portion a fairly large stone could be readily palpated with the palm of the left hand behind the second portion of the duodenum. The stone was firmly lodged near the anterior surface of the pancreas and therefore was attacked through an anterior transpancreatic approach. With the palm of the left hand behind the duodenum and with upward pressure against the stone by the index finger behind the pancreas, careful separation was made of the pancreas over the stone, the duct incised and the soft stone dislodged in pieces. Large amounts of stony material were washed out. With expulsion of the central fragments a foreign body extruded. This had a bulbous tip at one end and resembled in size and shape a partly decomposed cherry stem (shown in illustration). Catheters were sutured into the common duct openings. The patient made an uneventful recovery.

Dr. H. E. Evans, pathologist at the Los Angeles General Hospital, reported that the foreign body was a black structure



Foreign body and some of the fragments of stone removed from the common duct (twice natural size.)

2.5 cm. long and 2 mm. in width and less than 1 mm. in thickness and had the appearance of some sort of vegetable or plant matter. A section was submitted to Dr. E. M. Hall, professor of pathology at the University of Southern California School of Medicine. His report stated that sections showed a number of small bits of moderately woody plant tissue and that many tracheal ducts were present with fairly thick walls.

The patient was a bright chap, a student of chemistry at the University of Southern California, and during his convalescence we asked him whether he had knowledge of ever eating cherries, stem and all. He replied that cherries had always been his favorite dish and that in earlier youth he had often eaten them by the double handful, at times not paying too much attention to stem or stone. We felt that we were safe in assuming that this was a cherry stem which had been ingested and by accident had slipped up the ampulla and had become lodged in the common duct, in time to become the nucleus for a stone.

COMMENT

Foreign bodies in the biliary tract are seldom encountered and are indeed a curiosity. A recent article by Toland¹ reviews the literature quite thoroughly. Among some of the foreign bodies removed from the common duct were swabs, rubber drains and nonabsorbable catgut ligatures, all from previous operations. As a nucleus for stones, pieces of suture were found most frequently, followed by an incidence each of bristle,

thread and a piece of rubber drain. There are two reports of swallowing and migration: one a piece of wire and the other the handle of a spoon.

It is quite likely that if the centers of all single common duct stones were examined, particularly those occurring in apparently normal gallbladders without stones, the presence of a foreign body would be encountered at least occasionally.

523 West Sixth Street.

Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

THE ANTERIOR LOBE OF THE HYPOPHYSIS IN INTERMEDIARY METABOLISM

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This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—Ed.

The role of the anterior lobe of the pituitary in intermediary metabolism, especially in carbohydrate metabolism, has been reviewed by Houssay,¹ Russell,² Long,³ Van Dyke,⁴ Young,⁵ Thomson and Collip⁶ and others in recent years, in greater detail and with fuller bibliography than is possible in these pages. The subject is one of the greatest difficulty and complexity, since it is seldom possible to tell how widely the repercussions of any experimental interference may spread through the endocrine system. Great variations in behavior between species and between individuals in any one species are the rule rather than the exception. None of the anterior pituitary principles has yet been obtained in a state of indubitable purity, and any extract of the gland may or may not, depending on the source and the method of preparation, contain not only the thyrotropic and the corticotropic (adrenotropic) hormone (which must secondarily influence metabolic processes in many ways), the growth-promoting hormone (which presumably promotes anabolic processes even if its primary influence is on skeletal growth) and prolactin (which may directly or indirectly control metabolic adaptations to lactation) but also an uncertain number of principles active in metabolism but less clearly defined

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at present. For example, O'Donovan and Collip⁷ demonstrated the existence of a factor which rapidly elevates the metabolic rate and depresses the respiratory quotient in normal and in thyroidectomized rabbits and guinea pigs and which is apparently derived from the pars intermedia, being closely associated with the melanophore-expanding hormone. Extracts which contain this factor may be largely freed from the "accepted" pituitary substances by exposure to high temperatures and still display manifold effects on intermediary metabolism. Even true posterior lobe principles (known and unknown) may be present in so-called anterior pituitary extracts, and may be overlooked.

A comparatively simple example of the apparent contradictions which abound in this field of study may be given. The hypophysectomized animal, with its atrophic thyroid, has a low metabolic rate, and its peripheral tissues consume abnormally small amounts of dextrose at all blood sugar levels⁸; in other words, its tolerance for injected dextrose is low,⁹ but since the rate of absorption from the intestine is also greatly reduced, the tolerance for orally administered sugar is high.¹⁰

FASTING HYPOGLYCEMIA AND THE GLYCOSTATIC PHENOMENON

Many observers have noted that when hypophysectomized animals of any species are caused to fast, the blood sugar falls rapidly to levels dangerously low. In hypophysectomized monkeys, for example, after eighteen hours' fast the blood sugar averaged 59 mg. per hundred cubic centimeters, while in normal animals it was still 110 mg.;¹¹ and in rats, whose metabolism is more intense, the blood sugar concentration may be halved in eight hours' fasting after hypophysectomy, whereas controls show only a 20 per cent decrease.¹² Many hypophysectomized animals have died in hypoglycemia, and many have been dramatically resuscitated from a cold and deathlike torpor by injections of dextrose.¹³ The phenomenon is not ascribable to a breakdown of the mechanism of glycogenolysis, since the stores of liver glycogen usually show similar rapid exhaustion. It has been claimed¹⁴ that injected thyroxine will maintain the blood sugar of hypophysectomized animals during fasting, but it is more widely believed that the tendency to hypoglycemia is a consequence of the atrophy of the adrenal cortex which follows hypophysectomy, since adrenalectomized animals also show this tendency, especially if their mineral metabolism is con-

trolled, and since injected cortical steroid substances will protect both hypophysectomized and adrenalectomized animals against it.¹⁵

Two rival interpretations of the hypoglycemic tendency have been put forward. On one hand, it is urged that the hypophysectomized (or adrenalectomized) animal prefers carbohydrate as a fuel and is spendthrift of its stores thereof. Evidence for this is seen in experiments in which dextrose is administered orally to rats which have fasted for twenty-four hours; the normal rat will oxidize about half the dextrose administered (in the following four hours) and will store about one third of it as liver and muscle glycogen in roughly equal shares, but the adrenalectomized or hypophysectomized rat will oxidize more and store less, whereas administration of adrenal cortex extract increases storage.¹⁶ On the other hand, hypoglycemia may be an indication that the supply of new carbohydrate by glyconeogenesis is lagging behind the demands of the peripheral tissues. That the supply is, in fact, reduced after hypophysectomy is indicated by an analysis of blood leaving the liver;¹⁷ furthermore, if one makes the orthodox assumption that a large and fairly constant proportion of the amino acids liberated in the breakdown of tissue protein constitutes the main source of new carbohydrate for the fasting animal, the excretion of nitrogen becomes a measure of the intensity of glyconeogenesis and shows the latter to be restricted after hypophysectomy. During fasting the nitrogen excretion tends to be low,¹⁸ and is raised by the hormones of the adrenal cortex when they maintain the blood sugar level;¹⁶ the increase in nitrogen excretion and in stored carbohydrate which occurs when rats are exposed to low atmospheric pressures is not seen after extirpation of the hypophysis or of the adrenal cortex.¹⁹ There is, then, fair if not conclusive evidence that the fall in blood sugar and liver glycogen in fasting hypophysectomized animals indicates that a decrease in the production of hormones in the adrenal cortex has made impossible acceleration of the protein breakdown to a point at which glyconeogenesis would be adequate; and in any case the protective action of anterior pituitary extracts may be ascribed tentatively to the corticotrophic factor which they contain.²⁰

But the fasting hypophysectomized rat or mouse (other species have hardly been examined) shows a decrease in muscle glycogen which is more striking and appears more rapidly after extirpation of the gland than that in adrenalectomized animals; moreover, anterior pituitary extracts may display a "glycostatic" power to retard this decrease even when they contain little corticotrophic substance and even in rats which have been adrenalectomized as well as hypophysecto-

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mized.²¹ During an eight hour fast the concentration of muscle glycogen may fall from 0.55 to 0.50 per cent in a normal rat and from 0.50 down to 0.30 per cent in a hypophysectomized rat; the higher respiratory quotient of the latter shows that the vanished carbohydrate has been oxidized, while the nitrogen excretion affords no evidence that glyconeogenesis diminished.²² It is tempting to speculate that this using-up of muscle glycogen is due to a deficiency in the supply to the peripheral tissues not merely of dextrose, as in the adrenalectomized animal, but also of some other fuel (acetoacetic acid, for example; in which case this might be the inverse of the ketogenic phenomenon discussed later), but there is no supporting evidence at present for any such interpretation. It must be noted also, as a type of synergism yet unexplained, that the glycostatic phenomenon is most easily obtained when adrenal cortical principles are present in quantity, though it does not require that the gland itself should be intact.²⁰

SENSITIVITY TO INSULIN AND THE GLYCOTROPIC PHENOMENON

The extreme sensitivity of the hypophysectomized animal to insulin, observed by Houssay and Magenta²³ in the dog, has been confirmed in many other species; it is from ten to thirty times greater than that of intact animals, the hypoglycemia being both intense and prolonged. Some increase in sensitivity is also observed in animals deprived of their adrenal medullae or of the sympathetic nervous system or even of the thyroid gland; but these observations seem irrelevant in face of the fact that pretreatment with suitable anterior pituitary extracts may decrease the exaggerated response to insulin of the hypophysectomized animal²⁴ and completely prevent insulin hypoglycemia in the normal animal;²⁵ this is called the "glycotropic" effect. In attempting an interpretation one must bear in mind that extracts showing glycotropic activity do not raise the blood sugar level or affect carbohydrate stores in normal animals, do not prevent the development of hypoglycemia in fasting hypophysectomized animals²⁶ and do not retard the fall in blood sugar that follows hepatectomy in the rabbit (though they prevent further acceleration of this fall by insulin²⁷). Hence the factor is not a general inhibitor of carbohydrate consumption but a rather specific "anti-insulin"; yet any chemical interaction between these agents is unlikely, since the

glycotropic factor must be administered some hours before the insulin to be effective. Part of the sugar which disappears from the blood under the influence of insulin is laid down in the muscles as glycogen, and it is possible that the glycotropic factor prevents this.²⁶ Beyond this the attempt at interpretation becomes frankly speculative; one could, for instance, work out a hypothesis equating the glycotropic and ketogenic effects, while, on the other hand, Jensen and Grattan^{25d} produced evidence that the glycotropic and corticotropic factors are identical.

It was formerly thought that hypophysectomized animals were resistant to the hyperglycemic action of epinephrine and that this might explain their sensitivity to insulin, but it is only when the solution of epinephrine hydrochloride is injected subcutaneously that the sluggish circulation of the hypophysectomized animal, with its atrophic thyroid, prevents epinephrine from acting with its usual vigor.²⁸ Pretreatment with certain pituitary extracts diminishes the response to epinephrine; this is due to the presence of an unidentified factor probably originating in the posterior lobe.²⁹

EFFECT OF HYPOPHYSECTOMY ON PANCREATIC DIABETES

No discovery has more sharply focused attention on the role of the anterior lobe of the hypophysis in carbohydrate metabolism than that of Houssay and Biasotti,³⁰ who showed, first in toads and then in dogs, that hypophysectomy profoundly modifies and moderates the intense diabetes usually produced by complete pancreatectomy; this discovery has been repeatedly confirmed and extended. Survival without insulin is greatly prolonged, and the animals are as likely to die in a hypoglycemic crisis as from diabetes; glycosuria and hyperglycemia do not become extreme, and are controlled by small amounts of insulin; ketosis is slight or absent; metabolic rate and nitrogen excretion do not show the usual increase, and weight is lost slowly if at all; liver glycogen stores are quite well maintained, and although the tolerance to administered dextrose is quite low,³¹ excretion is not quantitative, and the respiratory quotient is not pegged at the fat level, while during fasting the low values of the urinary dextrose-nitrogen ratio indicate that much of the carbohydrate produced by glyconeogenesis is being consumed.

Long and Lukens^{32a} showed in cats and dogs that adrenalectomy affected pancreatic diabetes in much the same way as hypophysectomy did in Houssay's experiments, and they proved that it was the cortex rather than the medulla of the adrenal which was of importance. Their animals received cortical extract in quantities sufficient to prevent serious disturbance of water and salt metabolism but apparently insufficient

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to replace the function of the glands in carbohydrate metabolism; in later experiments they found that adrenalectomy abolished glycosuria in partially depancreatized rats, maintained after the second operation with saline solution.³ The effect of thyroidectomy on pancreatic diabetes is slight and inconstant.

Discussion of these adrenal-pituitary relations will be deferred until the action of pituitary extracts on animals doubly operated on has been described, but it may be well to point out here that while in the dog and still more in the cat pancreatectomy alone produces exceedingly severe and rapidly fatal diabetes, there are other species (including pig, sheep and monkey) in which the diabetes is of a relatively mild type, with low dextrose-nitrogen ratios, little ketosis and great sensitivity to insulin—resembling the condition observed in the hypophysectomized-depancreatized, or "Houssay," dog or cat, or clinical diabetes of moderate severity. It is especially interesting to note that cases have been encountered in the clinic in which fibrotic or other change had almost completely obliterated the islet tissue of the pancreas, yet the diabetes resembled that produced by pancreatectomy in the monkey³³ rather than that in the dog, and was less severe than in many other cases of clinical diabetes in which there was little or no pathologic alteration of the islets.

DIABETOGENIC ACTION OF ANTERIOR PITUITARY EXTRACTS

The injection of anterior pituitary extracts of many kinds is not infrequently followed by slight transient hyperglycemia; this has been ascribed to contamination with posterior-pituitary principles or to nonspecific stimulation of epinephrine discharge, and does not in any way merit the name "diabetogenic." But if fresh simple extracts that have been cautiously prepared are administered in large doses day after day to well nourished dogs, cats or rabbits, one may observe in many individual animals after some days a gradual but maintained rise of the blood sugar beyond glycosuric levels, moderate ketonuria, increased excretion of nitrogen and other symptoms of diabetes.³⁴ At its height the condition may simulate in severity that produced by pancreatectomy, from which it differs chiefly in maintenance of body weight, maintenance of liver glycogen and resistance to insulin treatment.⁵ It is interesting to compare this with the resistance to insulin exhibited in those patients with diabetes in whom acromegaly and hyperthyroidism point to hyperfunction of the anterior lobe of the pituitary as the primary disturbance. Yet it must not be supposed that the secretion of insulin continues unimpaired during the temporary diabetes produced by anterior pituitary extracts, for degranulation and hydropic degeneration of the beta cells of the islets of Langerhans occur,³⁵

the amount of insulin extractable from the pancreas falls to a low level,³⁶ and when such a pancreas is transplanted into a diabetic animal it seems to produce little insulin.³⁷ It seems unlikely that the anterior pituitary extract should have a directly harmful influence on the pancreas and more probable that the islets become exhausted because of the tendency of substances in the pituitary extract to elevate blood sugar and neutralize insulin action; similar changes in the islets are observed when blood sugar levels are kept high by injections of dextrose,³⁸ and a supply of extra insulin may protect the islets against the anterior pituitary extract.³⁹

Extracts which are diabetogenic in the dog have no such action in the guinea pig, mouse or rat; in the last, indeed, they cause a considerable increase in the quantity of islet tissue found in the pancreas and in the amount of insulin extractable therefrom;⁴⁰ this "pancreatotropic" effect is not now obtainable in the circumstances in which it was first described.⁴¹ One concludes that in some species the islet tissue is sufficiently adaptable to bear any strain that has yet been thrown upon it.

The type of experimental diabetes described in the foregoing paragraphs is well called temporary. Not merely does it soon subside after the treatment has ceased, but it does not persist for more than a few days even when the injections are continued at a constant level; the diabetic symptoms vanish, though resistance to insulin (glycotropic effect) persists. But an increase in the amount of anterior pituitary extract given will reestablish the diabetic state for a few days more, until finally a dose is reached (say, the equivalent of 25 Gm. of fresh gland daily) at which the animal can no longer escape: the diabetes not only persists as long as treatment continues but reaches a point (often marked by transient exacerbation of ketonuria) at which the degeneration of the islets becomes irreversible, so that the diabetes continues indefinitely and unabated even when the extract is withdrawn.⁴²

Such permanently diabetic dogs vary in the intensity of diabetes exhibited, but in general their insulin requirements, sugar excretion and dextrose-nitrogen ratios are even higher than those usually recorded for depancreatized dogs on the same diet; ketonuria, however, may be low in the early stages, weight is better maintained, and survival without insulin is much longer;⁴³ the islet tissue is altered to a variable extent,

33. Collip, J. B.; Selye, Hans, and Neufeld, A. H.: Experimental Pancreatic Diabetes in the Monkey, *Am. J. Physiol.* **119**:332 (June) 1937; *Canad. M. A. J.* **27**:287-288 (Sept.) 1937.

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35. Richardson, K. C., and Young, F. G.: Histology of Diabetes Induced in Dogs by Injection of Anterior-Pituitary Extracts, *Lancet* **1**:1098-1101 (May 14) 1938. Richardson, K. C.: Influence of Diabetogenic Anterior Pituitary Extracts on the Islets of Langerhans in Dogs, *Proc. Roy. Soc., London, s. B* **128**:153-169 (Jan. 4) 1940.

36. Best, C. H.; Campbell, James, and Haist, R. E.: Effect of Anterior Pituitary Extracts on the Insulin Content of the Pancreas, *J. Physiol.* **97**:200-206 (Dec. 14) 1939.

37. Houssay, B. A., and Foglia, V. G.: Diabetes antero-hipofisaria y función endocrina pancreática, *Rev. Soc. argent. de biol.* **12**:237-252 (Aug.) 1936.

38. Woerner, C. A.: Studies of Islets of Langerhans After Continuous Intravenous Injection of Dextrose, *Anat. Rec.* **71**:33-57 (May 25) 1938.

39. Campbell, James; Haist, R. E.; Ham, A. W., and Best, C. H.: Insulin Content of the Pancreas as Influenced by Anterior Pituitary Extract and Insulin, *Am. J. Physiol.* **129**:P328-P329 (May) 1940.

40. Richardson, K. C., and Young, F. G.: Pancreatotropic Action of Anterior Pituitary Extracts, *J. Physiol.* **91**:352-364 (Dec. 14) 1937. Marks, H. P., and Young, F. G.: Pancreatotropic Action of Anterior Pituitary Extracts, *Chem. & Industry* **58**:652, 1939.

41. Anselmino, K. J.; Herold, L., and Hoffmann, F.: Ueber die pankreatotrope Wirkung von Hypophysenvorderlappenextrakten, *Klin. Wchnschr.* **12**:1245-1247 (Aug. 12) 1933.

42. Young, F. G.: Permanent Experimental Diabetes Produced by Pituitary (Anterior Lobe) Injections, *Lancet* **2**:372-374 (Aug. 14) 1937; *Preparation and Properties of Pituitary Extracts*, *J. Endocrinol.* **1**:339-355 (Nov.) 1937.

43. Best, C. H.: Production of Diabetes in Dogs by Anterior Pituitary Extracts, *Lancet* **1**:1444-1445 (June) 1938. Houssay, B. A.: Acción diabética de diversas hormonas, *Rev. Soc. argent. de biol.* **14**:297-307 (Aug.) 1938. Deh...

44. Richardson, K. C.: Histology of Anterior Pituitary Extract, *Am. J. Physiol.* **125**:188-195 (Jan.) 1939. Loubatières, A.: Recherches sur le diabète sucré permanent consécutif aux injections d'extrait de lobe antérieur d'hypophyse chez le chien normal, *Compt. rend. Acad. d. sc.* **208**:1933-1935 (June 12) 1939.

45. Marks, H. P., and Young, F. G.: Observations on the Metabolism of Dogs Made Permanently Diabetic by Treatment with Anterior Pituitary Extract, *J. Endocrinol.* **1**:470-510 (Dec.) 1939.

and hardly any insulin can be extracted from it; surgical removal of the pancreas may have little influence, once the permanent diabetes is established. One feels that if there are real differences between dogs that are diabetic because their islet tissue collapsed under treatment with an anterior pituitary extract weeks or months previously and dogs that are diabetic because the whole pancreas has been removed, such differences must be due to the loss of the pancreatic acinar tissue in the latter rather than to persistence of any extrapancreatic effect of the anterior pituitary extract in the former.

ANTERIOR PITUITARY EXTRACTS IN DEPANCREATIZED ANIMALS

It is probably desirable to restrict the term "diabetogenic" to extracts capable of producing temporary if not permanent diabetes in normal dogs,⁵ but it has sometimes been applied in a rather different way. To produce diabetes in normal animals, even in the susceptible individuals of relatively susceptible species, one requires large doses of extracts which have been carefully protected from the destructive action of heat or powerful reagents; but in subtotally depancreatized animals (even of resistant species such as the rat) or hypophysectomized-depancreatized ("Houssay") animals, diabetic symptoms can be elicited easily, or intensified if already present, with moderate doses of extracts of many kinds. The conclusion is inescapable that true diabetogenic potency involves the action of one or more very labile factors as well as of relatively stable factors that may be effective by themselves in animals deprived of all or most of their insulin-producing tissue.

Among these relatively stable factors one may certainly include the corticotrophic principle, for extracts which evoke intense glycosuria and ketonuria in hypophysectomized-depancreatized cats have little or no effect on adrenalectomized-depancreatized animals;^{32a} adrenal cortex extract causes glycosuria in subtotally depancreatized (but not in normal) rats.⁴⁴ But in the latter test the action of the cortical steroids is not as great when they are administered by themselves as when they are administered simultaneously with anterior pituitary extracts (a further example of the type of synergism already discussed²⁰); moreover, anterior pituitary extracts may evoke glycosuria in partially depancreatized adrenalectomized dogs;⁴⁵ hence the corticotrophic factor is certainly not the only one involved. In considering the identity of the labile factor or factors, one naturally thinks of the "growth hormone," which is closely associated with diabetogenic activity;⁴⁶ and it has been shown recently that even brief heat treatment largely destroys the striking power of fresh anterior pituitary extracts to increase the body glycogen of normal fasting mice.⁴⁷ In viewing the diabetogenic phenomenon as a whole one may cite the evidence (quoted in the discussion of the hypoglycemia of fasting animals) that anterior pituitary principles often tend to increase glycogenesis; one may be inclined also to credit them with the power to diminish the utilization of carbohydrate by the peripheral tissues,

even if this seems to elude direct demonstration,¹⁴ and one has, unfortunately, several different unsupported interpretations of the glycotrophic phenomenon to draw on as required.

THE KETOGENIC PHENOMENON

The urinary excretion of acetone bodies by the fasting or fat-fed rat, normally quite small, may be greatly increased by injecting anterior pituitary extracts;⁴⁸ there is a simultaneous rise in blood ketones, which is a more sensitive and dependable index of the phenomenon, since acetoacetic and hydroxybutyric acids are to some extent threshold substances. Parallel observations have been made in other species, including the mouse, guinea pig, rabbit, dog and man. The effect is lessened but not abolished after adrenalectomy.

A general discussion of this phenomenon has been published elsewhere;⁴⁹ there is good evidence that it indicates an increased outpouring of ketone bodies by the liver rather than a diminished utilization of them;⁵⁰ and in general the ketosis is accompanied by a transfer of fat from the depots to the liver, in which large quantities may accumulate.⁵¹ There is accordingly a good deal of support for the view that the phenomenon represents a general stimulation of fat catabolism beyond the capacity of the body to oxidize the ketonic final products. Yet other possibilities exist; fatty acids are not the only conceivable source of acetone bodies, and there may well be different types of ketonemia; if stimulation of fat metabolism does occur, it may be secondary rather than direct.

Shipley and Long,⁴⁶ for instance, have suggested that the primary effect of crude extracts of the anterior lobe may be to retard the breakdown of tissue protein so that the energy requirements of the body are met by drawing on preformed carbohydrate stores (which are rapidly exhausted to the point of hypoglycemia⁵²) and on the fat depots, whose overactive response may produce ketonemia. Some retardation of protein catabolism is, as already pointed out, required of a "growth hormone," and it has in fact been observed in many experiments.⁵³ At first sight this appears to be a bewildering contradiction of the thesis already developed, that anterior

48. Burn, J. H., and Ling, H. W.: Ketonuria in Rats on a Fat Diet After Injection of Pituitary (Anterior Lobe) Extract, *J. Physiol.* 69: xix (March 15) 1930; Excretion of Acetone Bodies on a Fat Diet as Affected by the Injection of Pituitary (Anterior Lobe) Extract and by Pregnancy, *Quart. J. Pharm. & Pharmacol.* 6: 31-38 (Oct.-Dec.) 1933.

49. Shipley, R. A., and Long, C. N. H.: The Ketogenic Phenomenon, *Endocrinology* 26: 900-905 (May) 1940.

50. Mirsky, I. A.: Source of Blood Acetone Resulting from Administration of Ketogenic Principle of Anterior Hypophysis, *Am. J. Physiol.* 115: 424-428 (April) 1936.

51. Best, C. H., and Campbell, James: Anterior Pituitary Extracts and Liver Fat, *J. Physiol.* 86: 190-203 (Feb. 8) 1936; Effect of Anterior Pituitary Extract on Liver Fat of Various Animals, *ibid.* 92: 91-110 (Feb. 16) 1938.

52. Mirsky, I. A.: Source of Blood Acetone Resulting from Administration of Ketogenic Principle of Anterior Hypophysis, *Am. J. Physiol.* 115: 424-428 (April) 1936.

53. Teel, H. M., and Cushing, Harvey: Studies in the Physiological Properties of Growth-Promoting Extracts of the Anterior Hypophysis, *Endocrinology* 14: 157-163 (May-June) 1930.

54. Fry, E. G., Long, C. N. H., and Ritter, H. B.: Aggravation of Pancreatic Diabetes by Adrenal Cortical Extract, *Am. J. Physiol.* 126: 497 (July) 1939.

55. Houssay, B. A., and Biasotti, A.: Acción diabetogena anterohipofisaria en perros sin suprarenales, *Rev. Soc. argent. de biol.* 14: 308-314 (Aug.) 1938.

56. Shipley, R. A., and Long, C. N. H.: Studies on the Ketogenic Activity of the Anterior Pituitary, *Biochem. J.* 32: 2242-2256 (Dec.) 1938.

57. Neufeld, A. H.; Scoggan, S. M., and Stewart, G. S.: Effect of Pituitary Preparations on the Total Body Glycogen, Water, Nitrogen, and Fat of Fasted Mice, *Endocrinology* 27: 132-136 (July) 1940.

pituitary extracts (especially those containing the corticotropic principle) stimulate protein breakdown and glyconeogenesis, and certainly it is probable that one is here dealing with another factor. It is quite possible that the balance is held by the islets of Langerhans; nitrogen retention will be favored as long as they continue to produce sufficient insulin, nitrogen loss when they break down under the stimulus. Thus Mirsky,⁵⁴ using the rate of increase of nonprotein nitrogen in the blood of nephrectomized dogs to measure the catabolism of protein, finds it to be increased by crude extracts of the anterior lobe in depancreatized (diabetic) animals but slightly decreased in normal ones.

A great deal of effort has been expended in the study of the chemical and physical properties of the factors described and in attempts to separate them by chemical means; the results are of great importance to those actually working in the field but are unfortunately so full of apparent contradictions that they can rarely be used to support general statements and have accordingly been given little attention in this review.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING CHAPTER, WHICH IS THE THIRD OF A SERIES ON AMPUTATIONS AND ARTIFICIAL LIMBS TO APPEAR IN THIS COLUMN. WHEN COMPLETED, THE SERIES WILL BE PUBLISHED IN THE FORM OF A HANDBOOK ON AMPUTATIONS. THE COUNCIL WISHES TO EXPRESS ITS APPRECIATION FOR THE COOPERATION OF ITS GROUP OF CONSULTANTS ON ARTIFICIAL LIMBS. THE COUNCIL IS REPRESENTED BY DRS. FRANK D. DICKSON, HARRY E. MOCK, FRANK R. OBER, S. PERRY ROGERS, PAUL STEELE AND PHILIP WILSON, AND THE ASSOCIATION OF LIMB MANUFACTURERS OF AMERICA IS REPRESENTED BY MESSRS. MCCARTHY HANGER SR., W. E. ISLE, JOSEPH A. SPIEVAK, DAVID E. STOLFE AND J. B. KORRADY.

HOWARD A. CARTER, Secretary.

CHAPTER III. SITES OF ELECTION FOR AMPUTATION

Certain "sites of election" are generally recognized as promising functional amputation stumps, and numerous methods of operation at different sites have been planned with the same objective of function. These sites may be considered in order from below upward.

1. LOWER EXTREMITY

Amputation of toes results only in the slight loss of spring to the gait provided by the final push-off of the toes in each step. The natural weight bearing areas of heel and metatarsal heads are undisturbed, muscular control of the foot is not seriously interfered with, and satisfactory leverage remains. No prosthesis is required.

Amputation through the metatarsals sacrifices the normal weight bearing surfaces beneath the heads of these bones. A plantar flap compensates somewhat by retaining soft tissue integuments physiologically adapted to weight bearing. Muscular control of the ankle is sacrificed no more than in amputation of the toes, although cutting through the short plantar muscles impairs further the support of the arch. Leverage is lost in proportion as the site of amputation progresses backward, and function decreases accordingly. Lisfranc's amputation through the tarsometatarsal joints is as far back as one can go without this loss of leverage becoming prohibitive. It must be remembered that these amputations are usually due to trauma and that the injured tissues seldom allow amputation at this level.

Amputations between the tarsometatarsal and the ankle joints are condemned. Chopart's amputation, leaving only the astragalus and the calcaneus, is the one most commonly employed. Two factors, loss of the natural attachments of the anterior tibial, peroneal and toe extensor muscles and further shortening of the lever of the foot, render equinus deformity of the stump almost inevitable. The appliance for such amputations is as unwieldy and unsightly as that for an amputation just above the ankle, and the resultant function is not so good.

Amputations immediately above the ankle joint are called Syme's or Pirogoff's. In both operations the tibia and fibula are sawed horizontally within 1 inch of the ankle joint. Both employ a posterior flap composed of all the layers of soft tissue from the tip of the heel, and both leave a transverse anterior scar. In Pirogoff's technic the posterior part of the os calcis, sawed vertically, is left in the flap and is opposed to the cut surface of the tibia. Both amputations require careful surgical technic in care of the vessels and nerves and in snug tailoring of the flaps. Neither is likely to succeed in the presence of infection.

Amputations at this level were in high favor a century ago. The patient could frequently walk, or even run, without any appliance. The prosthesis is bulky. It must be entered from the front and laced snugly above the bulbous tip of the stump. It is more serviceable without any ankle joint mechanism. Modern limb manufacturers hold in disfavor any amputation between the heads of the metatarsals and the middle of the leg because of the unsightly appearance of the prosthesis. A recent English compilation of late results in Syme amputations performed during the war of 1914-1918 shows that almost all of these stumps have now been reamputated because of circulatory complications.

The optimum site for amputation in the shaft of the leg is its middle third. In the adult this will vary between 5 and 7 inches from the joint line, depending on the height of the patient and the length of the limb. Longer stumps are apt to be insufficiently covered, to be tender and to suffer vascular difficulties. Longer stumps also require an unsightly bulkiness in the shank of the prosthesis. The shorter stumps, cut through cancellous bone, are likely to permit a larger degree of end bearing, although most of them require that the greater part of the weight be borne on the sloping surfaces of the head of the tibia. The minimum length of tibia for satisfactory leverage is $2\frac{1}{2}$ inches. The fibula should usually be retained for its function in controlling rotation of the prosthesis. In very short stumps it may be removed entirely. If retained it should be cut from 1 to 2 inches shorter than the tibia, depending on the length of the stump. In children the fibula should be cut three inches shorter or else its epiphysis should be arrested. If the fibula is removed, care should be exercised to remove all its periosteum as well.

Amputation through the leg is conveniently performed with the patient prone (face downward). The bones should be denuded of periosteum for a distance of 1 inch and all sharp corners removed, the anterior border of the fibula with a saw and all sharp edges with a rasp. The bones should be covered with a posterior flap composed of the tendinous aponeurosis of the gastrocnemius and fascia with little or no muscle, and in turn by an anterior skin flap long enough to leave a posterior scar. Redundance of flaps must be avoided. Postoperative splinting is especially important to prevent contracture of the knee. Massage, active exercise

54. Mirsky, I. A.: The Influence of the Anterior Pituitary Gland on Protein Metabolism, *Endocrinology* 25:52-56 (July) 1939.

and hardening of the stump are recommended. Early walking on a temporary prosthesis is advantageous.

Amputation by disarticulation at the knee joint, popular a century ago, has fallen into such disuse that it is now generally employed only as a temporary emergency procedure. Objections based on mechanical reasons, such as bulkiness and unsightliness of the prosthesis, and the necessity of disproportionate length of thigh and leg, are unfounded under modern facilities of artificial limb manufacture. Some disarticulation stumps have been unsatisfactory from the functional standpoint for one of two reasons: The patella floating free on the front of the thigh may remain so tender as to prohibit encasement in a socket. Other stumps have permitted painless end bearing at first only to undergo atrophy and ulceration of the terminal integuments after months or years of function.

Theoretically, numerous physiologic and mechanical advantages are apparent at this level. The femoral condyles and the patella, as well as all the soft tissues in an anterior flap, are physiologically adapted to withstanding pressure. Ligation of the popliteal artery below its superior genicular branches leaves a rich anastomosis of vessels at the end of the stump. Retention of the lower femoral epiphysis assures normal growth of the stump in a child. Recent modifications in operative technic, described by Rogers, are directed against the previous faults in these stumps. Arthrodesis of the patella to the front of the femur in its anatomic position eliminates any tenderness and increases the end bearing surface area. Fixation of all the hamstring tendons to the tip of the patellar tendon in the posterior intercondylar notch relieves the terminal soft tissues of tension and subjects them only to pressure, which they are adapted to bear. A limited experience with this technic promises relief from the late complications previously encountered in some amputations at the knee joint.

Amputations through the supracondylar region of the femur are best made with a long anterior flap and a posterior scar. A large degree of end bearing is provided by the osteoplastic method of Gritti-Stokes and by the tendinoplastic methods of Callander and of Kirk. The English experience with a large number of osteoplastic amputations performed between 1914 and 1918 shows that most of these stumps have broken down after some years and been reamputated at a higher level. The composite experience of American limb manufacturers shows that whenever the technical details of the operation were carried out originally the incidence of reamputation has been very small. The tendinoplastic procedures with long flaps and loose closure are particularly suitable in the presence of infection or circulatory impairment. Limb manufacturers prefer to have these stumps 3 inches shorter than the opposite femur for two reasons: to allow room for an internal knee-joint mechanism and to permit the use of a conical socket which can be entered from the top.

The physiologic factors in amputation through the shaft of the femur are similar to those through the leg. Partial end bearing is sometimes possible but most of the weight must be taken on the ischial tuberosity. Sensitiveness to the side pressure of leverage is likely to be less than in the leg because the femur is covered in its whole circumference. Muscles attaching high on the bone exert sufficient voluntary control provided the stump is long enough to transfer that motion. The prosthesis must be suspended from the shoulders or pelvis, and short stumps need a pelvic band. Function

may be limited by the weight bearing surfaces available and by the instability of the flabby stump within the socket.

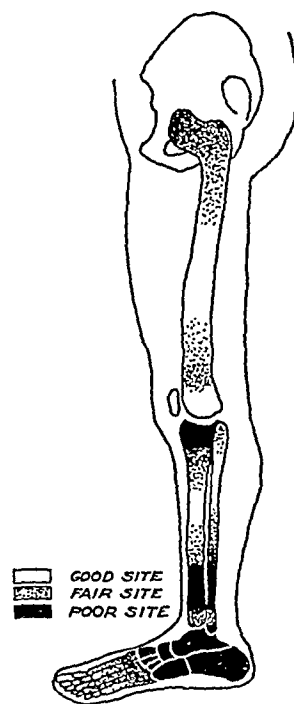
In amputations through the shaft of the femur the rule is to leave as much bone length as possible. The bone should be denuded of periosteum and rounded off with a rasp, as in the leg. The bone end should be covered with fascia or tendon but not with muscle. An anterior skin flap is best, though it need not be a long one to fall behind the end of the bone. Flaps should be sufficient but not redundant. An artificial limb can be applied at an early date.

In disarticulation of the hip, muscular control again becomes more difficult because one more joint is gone, but weight bearing becomes more single because the ischium, and in fact the entire buttock, can sit firmly in a bucket. Control of the entire extremity is afforded only by motions of the pelvis. Disarticulation of the hip is recommended only in case of necessity. Any thigh stump assures better function than a disarticulation. Whenever possible, sufficient muscle should be preserved to provide a cushion for bearing in an artificial leg. Such amputations can be fitted and many such legs are handled very well. It is especially important to get such an appliance early and to prohibit the postoperative use of crutches in order to avoid the crutch habit.

2. UPPER EXTREMITY

The rule for amputations within the hand is to preserve every bit of every kind of tissue possible for later reconstructive surgery if necessary. This rule, however, should be modified frequently by the consideration of saving function rather than form. There is no point, for instance, in saving individual fingers

which are so badly smashed that they can never be useful. The thumb falls in a different category because of its function in opposing all the fingers, so that even a stiff thumb in the opposed functional position is extremely valuable. Traumatic amputation of the tips of the fingers is well treated by immediate free full thickness skin grafts. In traumatic amputations of finger tips in which the base of the nail bed remains intact it is well to apply narrow adhesive traction strips over the end of the stump; the additional three weeks required to granulate and epithelize the wound is rewarded by a sound and sightly stump. If the entire nail bed is gone it is better to sacrifice enough bone to insure primary closure of adequate soft tissue flaps. In amputation of the middle and ring fingers a good part of the proximal phalanx must be retained in order to prevent lateral deformity of the index and little fingers developing at a later date; if the proximal phalanx cannot be retained, the distal third of the metacarpal should be removed. In loss of the little finger it is well to remove half of the meta-



Sites of election for amputation with expectant function in stump.

carpal in an oblique fashion so as to give a smooth contour to the ulnar side of the hand. In the index finger it is probably better to leave the head of the metacarpal. In the loss of the entire thumb or of all the fingers the situation is not hopeless if function of the remaining digit or digits is retained; either thumb or fingers can be replaced by artificial members against which the remaining movable members can act. The intricate and coordinated movements of the upper extremity cannot be duplicated in artificial limbs. This limitation, for instance, is the basis for disagreement concerning the site of election for amputation about the wrist. For the application of an appliance cosmetically resembling a hand, the forearm should be amputated at the junction of the middle and lower thirds, yet the majority of patients do not wear appliances on the upper extremity and many find the heel of the hand, some movable carpal bones, or even the bulge of the styloid processes useful in movements coordinated with the other hand. In general, it is agreed that as much length as possible is desirable in all amputations in the upper extremity. A terminal scar in the arm or forearm is satisfactory.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

AT THIS YEAR'S COUNCIL MEETING THE REFEREE FOR PREPARATIONS USED NASALLY CALLED ATTENTION TO THE INCREASING NUMBER OF REPORTS OF LIPID PNEUMONIA CAUSED BY THE USE OF OILY PREPARATIONS IN THE NOSE. AS A RESULT OF THE ENSUING DISCUSSION THE COUNCIL ASKED DR. PAUL R. CANNON TO PREPARE A PAPER ON THIS SUBJECT. DR. CANNON KINDLY CONSENTED AND THE COUNCIL ADOPTED THE APPENDED REVIEW FOR PUBLICATION.

PAUL NICHOLAS LEECH, Secretary.

THE PROBLEM OF LIPID PNEUMONIA

A BRIEF REVIEW

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It is now fifteen years since Laughlen¹ called attention to a type of pneumonia caused by the aspiration into the lungs of oily medicaments administered either intranasally or by mouth. Of the several names which have been applied to the condition, such as lipid pneumonia, lipid pneumonia, fat pneumonia, steatosis of the lungs, pneumonoliposis, lipid cell pneumonia, paraffin pneumonia, oil pneumonia and oil aspiration pneumonia, "lipid pneumonia," suggested recently by Graef,² seems to be the most appropriate. Although many phases of the subject have been clarified³ in the twenty-two or more papers which have been published in this country alone, the fact that so many unsuspected cases continue to be discovered at necropsy suggests that many persons, including physicians, are still unfamiliar with the conditions leading to its development.

The pneumonia varies greatly in severity, depending on the kinds and amounts of lipids aspirated. Some oils are markedly irritating and cause an acute edema and alveolitis with accompanying symptoms of cough and increased respiratory rate. Massive aspirations of oil have led to attacks of choking, cyanosis and suffocation, caused by the accumulation of large amounts of oil

in the alveolar spaces. Particularly serious also is the septic pneumonia which so frequently follows the aspiration of the lipid, owing presumably to the concomitant entrance into the lungs of the irritating oil and pathogenic micro-organisms. This condition is usually accompanied by fever and a persistent cough. In many instances of aspiration of lipids, however, the pulmonary damage is minimal and the symptoms are correspondingly slight or absent. This is particularly true when small amounts of liquid petrolatum enter the lungs. The harmful effects here result from the repeated entrance of the oil into the lungs, its accumulation in the air spaces and its prolonged irritating effect. This form of lipid pneumonia is serious because its development is so insidious. Finally, there are instances of lipid pneumonia in which diagnosis is made only by microscopic examination of the lungs. The demonstration of a few collections of lipophages in alveoli is obviously of little importance in itself; the real value of the observation lies in its proof of the ease with which light oils and fluids can pass from the upper respiratory passages to the lungs. This is perhaps the most important lesson which the study of lipid pneumonia has revealed.

OCCURRENCE AND PATHOGENESIS

Lipid pneumonia may occur whenever exogenous lipids enter the pulmonary tissues and remain there long enough to cause irritation. Its pathogenesis is the most important feature of the subject, because the disease can be prevented only by knowing what types of lipids enter the lungs and under what conditions.

The lipids most commonly concerned are of two main kinds: (1) those taken by mouth and (2) those introduced into the upper respiratory passages. The first group includes cod liver or halibut oil, castor oil, liquid petrolatum or milk fat; the second group comprises the various medicated oils that are used as intranasal sprays or nose drops. Some cases have been reported in which liquid petrolatum was used as a lubricant after tracheotomy or laryngectomy,⁴ and Garvin⁵ has reported an instance in which the patient allowed an oily salve to trickle down the throat daily over a period of about one month. In the cases reported by Davis⁶ and Houck,⁷ medicated liquid petrolatum was instilled directly into the trachea, and in one case the oil was used as a nasal douche, three or four times a day, over a period of nine years. It was estimated that during this time the patient had used more than 9 gallons of liquid petrolatum!

The earlier reports on the occurrence of lipid pneumonia led to the belief that it is essentially a disease of infants and children. Accumulated evidence has proved, however, that it affects all ages, and at least 105 cases, most of which were discovered at necropsy, have been reported in adults.⁸ The view, furthermore, that it occurs almost entirely in weakened individuals and particularly in those with defects of deglutition is no longer correct; it is now certain that healthy persons may develop severe types of lipid pneumonia, especially

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5. Garvin, C. F.: Lipoid Pneumonia: Report of Two Cases, Arch. Int. Med. **64**: 586-589 (Sept.) 1939.
6. Davis, K. S.: Roentgenographic Changes Following the Introduction of Mineral Oil in the Lungs, Radiology **26**: 131-137 (Feb.) 1936.
7. Houck, G. H.: Pulmonary Oil Tumors: Granulomata Caused by the Intratracheal Instillation of Liquid Petrolatum (Lipoid or Oil Aspiration Pneumonia), with Report of a Case, Medical Papers Dedicated to Henry Asbury Christian, Baltimore, Waverly Press, 1936, pp. 463-478.
8. Freiman, D. G.; Engelberg, Hyman, and Merritt, W. H.: Oil Aspiration (Lipoid) Pneumonia in Adults. A Clinicopathologic Study of Forty-Seven Cases, Arch. Int. Med. **66**: 11-38, July, 1940.

From the Department of Pathology, the University of Chicago.

1. Laughlen, G. F.: Studies on Pneumonia Following Naso-Pharyngeal Injections of Oil, Am. J. Path. **1**: 407-414 (July) 1925.

2. Graef, Irving: Studies in Lipid Pneumonia, Arch. Path. **28**: 613-667 (Nov.) 1939.
3. Pinkerton, J. S.; Ikeda, T.; Freiman, Engelberg and Merritt.⁸

if they use medicated liquid petrolatum intranasally in large quantities over long periods of time.

Aspiration of milk fat, fish oil or liquid petrolatum may occur under conditions which are difficult or at times impossible to control, as, for instance, in babies or debilitated adults who are recumbent for long periods of time. Aspiration of these lipids is further favored by conditions which interfere with normal processes of deglutition, such as cleft palate, convulsions, spasms, frequent attacks of gagging or vomiting, cerebral birth injuries and congenital neurologic disorders. Similarly, in adults who use liquid petrolatum for the relief of constipation, pulmonary aspiration may be favored by dysphagia caused by nervous disorders, cerebral hemorrhage, brain tumors, or by local inflammations or neoplasms of the mouth, throat, larynx or esophagus.

Of particular interest, because it is more easily controlled, is the type associated with the intranasal use of medicated liquid petrolatum. This form of therapy is widespread, not only in medical practice, but also in home medication. Although physicians are beginning to discourage the custom, many persons continue to use the "nasal oils" because of the extensive advertising campaigns of the makers. One company, over the radio, urges every one with symptoms of a beginning cold to put "a few drops in each nostril" when needed. No warning is given as to the possible harm resulting from their excessive or habitual use. Abandonment of this type of medication will be slow because of the fact that so many persons have used oily nose drops with no apparent ill effects. This, however, no more indicates the harmlessness of the practice than does the occasional ingestion of small amounts of lead prove that it is not a poison and can therefore be eaten repeatedly over a long period.

It is particularly regrettable that liquid petrolatum was selected as the solvent for various medicaments in the treatment of infections of the upper respiratory tract. This oil was chosen mainly because of the belief that it is "bland," is nonirritating, does not become rancid, spreads easily, and prevents drying and crusting of the respiratory surfaces. It was not realized how readily the oil, under certain conditions, can enter the lungs and that the persistent use of a few drops a day over a period of days and weeks can lead to the entrance of considerable quantities. Walsh and Cannon⁹ have cited the directions given by one manufacturer that "for children from six months to ten years of age the dosage is one-half dropperful in each nostril three or four times a day." As this dropper contained 1.5 cc., a six months old child would receive a total dose of from 4.5 to 6 cc. a day, or more than an ounce a week. If only a third of this got into the small lungs of a baby, a large area of pulmonary tissue would necessarily be affected. The most unfortunate aspect of the problem, however, is the fact that liquid petrolatum cannot be metabolized by tissue enzymes as can some of the animal and vegetable oils and hence remains as a foreign body irritant. This effect in subcutaneous tissues is well known as the so-called paraffinoma. Its similar effect in the pulmonary tissues caused Ikeda¹⁰ to designate this type of lipid pneumonia "paraffinoma of the lung."

MODE OF ENTRANCE INTO THE LUNGS

Liquid petrolatum, either when instilled or when sprayed into the nostrils, may enter the lungs in varying amounts, depending on the dosage, the frequency with

which it is applied and the extent to which the epiglottis functions effectively. It reaches the lungs fairly easily, however, because, being light, it does not elicit the cough reflex but enters the glottis and is aspirated or allowed to gravitate into the alveolar spaces. This is especially likely to happen during sleep if the oil has been used before retiring, as shown by the demonstration by Quinn and Meyer¹¹ that iodized poppy-seed oil instilled into a patient's nose during sleep could be readily demonstrated in the bronchial tree. Although probably only a small proportion of the oil enters the lungs, the remainder being swallowed, long-continued use may lead, eventually, to its accumulation in considerable quantities, because, once within the alveolar spaces, comparatively little resorption apparently occurs. This fact is strikingly shown in the case reported by Fischer-Wasels¹² of a 70 year old woman who was thought to have a tumor of the lungs. At necropsy, however, it was discovered that the supposedly neoplastic masses contained large quantities of a non-saponifiable oil. Inquiry revealed that this woman, for many years, had had the daily habit of spraying her nasal passages with large amounts of a mentholated liquid petrolatum. Similar cases have since been reported.¹³ Fischer-Wasels suggested that the menthol in these preparations may act as a mild local anesthetic and thus lessen the tendency for the cough or gag reflex to prevent the entrance of the oil into the trachea.

PATHOLOGIC EFFECTS IN THE LUNGS

The effects of this entrance of foreign lipids may be acute or chronic, localized or diffuse. The oils are all irritating, although in varying degree, and may cause inflammatory changes ranging from simple congestion and edema to necrosis. Pinkerton¹⁴ demonstrated quite clearly that the animal oils, particularly cod liver oil, are highly irritating, whereas some of the vegetable oils, such as olive oil, cottonseed oil, sesame oil and poppy-seed oil, are relatively nontoxic. This blandness of vegetable oils is of practical importance in that iodized poppy-seed oil has been so useful in bronchography and has apparently led to no serious after-effects in the lungs.¹⁵ Pinkerton suggested that the greater tissue-damaging effect of the animal oils may be due to their greater hydrolytic cleavage into irritating fatty acids. He observed, however, that chaulmoogra oil is markedly toxic to pulmonary tissues, and Graef² has recently pointed out that several of the vegetable oils, notably croton oil, castor oil and peanut oil, are exceedingly active tissue irritants. There is no doubt, however, that cod liver oil is extremely injurious to pulmonary tissues and its aspiration has been followed by severe cases of lipid pneumonia, some even with abscess formation.¹⁶

Liquid petrolatum, although less acutely damaging than the aforementioned oils, is far from bland. Experiments performed by Cannon and Walsh¹⁷ showed that

11. Quinn, L. H., and Meyer, O. O.: The Relation-ship of Sinusitis and Bronchiectasis, *Arch. Otolaryng.* **10**: 152-165 (Aug.) 1929.

12. Fischer-Wasels, B.: Tödliche Lungenschrumpfung durch Gebrauch von Mentholöl, *Frankfurt Ztschr. f. Path.* **44**: 412-425, 1933.

13. Gaertner, K.: Feler Paraffingranulome in der Lunge, *Frankfurt Ztschr. f. Path.* **51**: 98-103, 1937. Ball, F. E.: Petrolatum Oil Pneumonia, *J. An. Adult.* **1**: 69-62-65 (Jan.) 1936. Bodmer, H., and Kallós, P.: Ueber schwere Lungenschädigung (Lungenirritation) infolge Aspiration von Paraffinöl bei therapeutischer Anwendung, *Arch. f. Ohren-, Nasen- u. Kehlkopfheilk.* **136**: 40-45, 1933. Bishop, P. C.: Oil Aspiration Pneumonia and Pneumolipidosis, *Ann. Int. Med.* **13**: 1327-1359 (Feb.) 1940. Walsh and Cannon⁹ Thomas and Rienthoff.²²

14. Pinkerton, Henry: The Reaction to Oils and Fats in the Lung, *Arch. Path.* **5**: 380-401 (March) 1928.

15. Wright, R. D.: Reaction of Pulmonary Tissue to Lipiodol, *Am. J. Path.* **11**: 497-501 (May) 1935.

16. Cannon, P. R.: Lipoid Pneumonia, *Arch. Path.* **19**: 135-136 (Jan.) 1935.

17. Cannon, P. R., and Walsh, T. E.: Lipoid Pneumonia and Some Potential Dangers of Intranasal Medication, *Internat. Clin.* **3**: 109-115 (Sept.) 1938.

9. Walsh, T. E., and Cannon, P. R.: The Problem of Intranasal Medication, *Ann. Otol., Rhin. & Laryng.* **47**: 579-607 (Sept.) 1938.

10. Ikeda, Kano: Lipoid Pneumonia of the Adult Type (Paraffinoma of the Lung), *Arch. Path.* **23**: 470-492 (April) 1937.

the intranasal instillation of purified liquid petrolatum into healthy rabbits caused the development of acute pulmonary edema, proving that the oil in the lungs can injure capillaries sufficiently to cause increased capillary permeability and the leakage of albumin into the alveolar spaces. This fact has a definite bearing on the intranasal use of medicated liquid petrolatum in infants and young children with acute infections of the upper part of the respiratory tract. Under these conditions it is probable that whatever oil enters the lungs carries with it bacteria or viruses, and these, because of the edema induced by the oil, may find conditions more favorable for development, thus initiating a bronchopneumonia. In case of death all evidence of the early injurious effects of the oil in setting the stage for the terminal pneumonia might easily be obscured by the abundant inflammatory exudate.

The chronic effects in the lungs from the aspiration of liquid petrolatum are particularly severe, owing to the fact that it leads to the development of reticulum fibers, giant cells and, in time, abundant fibrosis. The subsequent formation of scar tissue is, consequently, as destructive to pulmonary integrity as is any other fibrosing process. It is likely, furthermore, to be more insidious, because the resultant persistent cough may lead to the more frequent use of nasal sprays or instillations in a further attempt to alleviate the cough.

Although the effects from the aspiration of oils are confined for the most part to the lungs and tracheo-bronchial lymph nodes, instances of blood stream dissemination are recorded¹⁸ in which liquid petrolatum has been found as encapsulated masses of oil giving the appearance of tubercle-like lesions in the spleen and liver. In the case reported by Young, Applebaum and Wasserman¹⁹ in which cod liver oil had been aspirated, renal lesions suggestive of periarteritis and diffuse glomerular nephritis were attributed to embolic blockage by oil droplets.

Microscopic demonstration of the presence of oily materials is usually simple although the differentiation of the kinds, and the determination whether they are endogenous or exogenous, is more difficult. With exogenous lipids the alveolar spaces are filled characteristically with large vacuolated mononuclear cells which at times have almost a signet-ring appearance. These so-called lipophages fill many air spaces and may at times be coughed up and identified in smears of the sputum. Liquid petrolatum can be partially identified by the fact that it stains with scarlet red but does not reduce osmic acid. It is also insoluble in absolute alcohol. Cod liver oil, on the other hand, reduces osmic acid and, as emphasized particularly by Pinkerton, forms characteristic acid-fast membranes at the edges of the oil masses which can be demonstrated by the Ziehl-Neelsen method. More complete and accurate identification of the oils is best made by chemical extraction of tissues, with subsequent determination of boiling points, iodine number, degree of saponification, acrolein reaction and specific color reactions. By these methods Pinkerton, Graef and Freiman, Engelberg and Merrit, particularly, have clarified several important details of the general problem. Similar chemical studies will add much valuable information concerning pathogenesis of lipid pneumonia in individual cases.

18. Pinkerton, Henry, and Moragues, Vicente: Paraffinoma of the Lung with Secondary Tubercle-like Lesions in the Liver and Spleen, *Arch. Path.* **29**: 691-699 (May) 1940. Pinkerton,²³ Young, Applebaum and Wasserman.¹⁹
19. Young, Anna M.; Applebaum, H. S., and Wasserman, P. B.: Lipoid Pneumonia: Report of a Case, *J. A. M. A.* **112**: 2406-2409 (June 10) 1939.

DIAGNOSIS

The diagnosis of lipid pneumonia, although usually not made ante mortem except in the severer cases, is possible at times. Of first importance is the history of the use of oily materials by mouth or in the nasal passages, with information as to amounts, duration and frequency of use. A persistent cough may be present, and in some instances there has been a history of choking attacks. Periods of low grade fever, due presumably to an accompanying septic pneumonia, have been observed. These symptoms, in conjunction with the physical observation of impaired pulmonary resonance and altered breath sounds, are informative, particularly if observed in a weak, debilitated or premature infant and in infants or adults with dysphagia from any cause.

Laboratory aids to diagnosis include the demonstration of oil laden macrophages in coughed up sputum or in tissue obtained by the bronchoscope for biopsy. Roentgenologists²⁰ have added considerably to the means of diagnosis by their demonstration of areas of increased density in the posterior, dependent portions of the lungs and in the perihilar regions with a tendency to be more marked on the right side. It is obvious, however, that these effects are evident mainly in patients with extensive and chronic involvement. Roentgenologists also emphasize the necessity for serial roentgenograms, particularly in the moderate and mild cases.

The chronic form of lipid pneumonia, especially that due to liquid petrolatum, must be differentiated from such conditions as pneumoconiosis, chronic bronchitis or bronchiectasis, chronic asthma, passive congestion, unresolved pneumonia, chronic fibroid tuberculosis, fungous infections of the lungs and bronchogenic carcinoma. Accurate differentiation is especially important with respect to the latter condition because of the increasing employment of surgery in its treatment. Errors in diagnosis here are particularly serious and, indeed, have already occurred. Rigler²¹ reported a case of unilateral lipid pneumonia in an adult which was diagnosed as bronchogenic carcinoma, and in the case reported by Thomas and Rienhoff²² pneumonectomy was performed on a 35 year old man on whom a diagnosis of carcinoma of the lung had been made. Death occurred from infection a few days later and the necropsy revealed a localized lipid pneumonia of the middle lobe of the right lung. It was learned later that "for over three years it had been the habit of the patient to apply medicated nasal spray with an atomizer, especially at night before retiring. The spray consisted of liquid petrolatum containing menthol and ephedrine." As so many adults are using oily nose drops and sprays by self medication, thoracic surgeons will need to give serious attention to the possible presence of chronic lipid pneumonia in the differential diagnosis of carcinoma of the lung.

INCIDENCE

It is impossible at present to ascertain the incidence of lipid pneumonia, and only certain inferences can be drawn from the evidence now available. The clinical effects vary greatly because of the different types and amounts of oils aspirated and, except in the severer cases, clinical diagnosis is therefore difficult. Most of the cases reported have been diagnosed at necropsy;

20. Pierson, J. W.: Some Unusual Pneumonias Associated with Aspiration of Fats and Oil in Lungs, *Am. J. Roentgenol.* **27**: 572-579 (April) 1932. Brown, R. S., and Wolman, I. J.: Lipoid Pneumonia in Infants and Children, *Radiology* **32**: 1-7 (Jan.) 1939. Davis.²
21. Rigler, Leo, in discussion on Davis.
22. Thomas, H. M., Jr., and Rienhoff, W. F.: Lipoid Cell Pneumonia, Adult Type, *South. M. J.* **32**: 1077-1080 (Nov.) 1939.

there are, no doubt, many more that have been overlooked or left unreported by pathologists. It is obvious that postmortem evidence alone can tell but little about the incidence of many kinds of disease. This is important to bear in mind because many physicians feel that, as so few necropsy cases have been reported, lipid pneumonia is a rare disease. By such logic, however, one would have to conclude that many diseases are rare, as for example morphinism, vitamin B deficiency or allergy. As the mild cases of lipid pneumonia are usually unsuspected, it is probably a more common malady than the nearly 200 cases which have been reported would indicate.

Furthermore, the incidence of lipid aspiration will vary directly with the extent to which pathologists make systematic routine histopathologic examinations of the lungs in every necropsy. Pinkerton²³ found 6 instances in 290 consecutive necropsies of infants and young children; Ikeda²⁴ found 7 in 101 consecutive necropsies. Freiman, Engelberg and Merrit,⁸ in attempting to ascertain the incidence among elderly patients with chronic disease, found 41 instances in 3,500 consecutive necropsies. We have found 39 instances in 2,000 consecutive necropsies, of which 12 were of infants and children and 27 of adults. These figures give a rough idea of the extent to which lipids may be aspirated, but it is obvious that the incidence of this aspiration must vary widely in different parts of the country and of the world, depending on the distribution of respiratory infections and the tendency of physicians and of the public to use medicinal oils.

PREVENTION

Lipid pneumonia, being essentially a man-made disease, can be prevented largely by the extent to which the conditions now known to favor its development are eliminated. In infants greater care can be paid to methods of administering fish oil and liquid petrolatum in order to avoid the hazards of aspiration, as for instance by the giving of smaller amounts per dose or by using concentrates. One of the great hazards can be removed by the elimination of all forcible feeding of cod liver oil or liquid petrolatum. The disastrous consequences of this practice have already been mentioned. Monfort²⁵ cites a case in which a 7 weeks old child in good health was forcibly given liquid petrolatum while crying. Soon after, the child developed a hacking cough, rapid respiration (86-88 per minute) with periods of apnea and with normal temperature and blood count. Roentgenograms revealed extensive bilateral infiltration in the hilar spaces. Eleven days later death resulted from bronchopneumonia. Greater care can also be given to the feeding of prematurely born or to weakened or debilitated infants.²⁶ Pinkerton warned against the practice of feeding such infants while lying on their backs, and Monfort has called attention to the need for abandoning the not uncommon practice of propping the nursing bottle on a pillow with the nipple remaining in the mouth. It is probable, therefore, that some cases of lipid aspiration can be prevented by giving more attention to these and other causative factors such as the feeding of comatose individuals, the use of gavage and the prevention and control of vomiting.

The problem of prevention of lipid pneumonia due to intranasal medication is more hopeful. Of the cases in

adults thus far reported in the literature, approximately 20 per cent were acquired because of intranasal medication, and in a series of cases including infants, children and adults, reviewed by Walsh and Cannon, approximately a third resulted from intranasal medication. It would seem advisable, therefore, to reexamine the rationale of local medication of the upper part of the respiratory tract in order to ascertain whether the benefits which may result from this mode of therapy outweigh the harmful effects now so well demonstrated in the massive natural experiment of lipid pneumonia.

Healy,²⁷ in discussing recently the problem of therapy in acute rhinitis, said "The ideal therapeutic aims of local medication in acute rhinitis are the reduction of nasal congestion, the promotion or restoration of ciliary function and the destruction of pathogenic organisms." He cited evidence from the work of Proetz,²⁸ Lierle and Moore²⁹ and Fenton and Larsell³⁰ that many of the commonly used nasal oils and so-called antiseptics actually impair or paralyze ciliary activity and even destroy respiratory epithelium. Walsh and I⁹ have discussed elsewhere the general problem of intranasal medication and have challenged the assumption that the solution of medicaments in liquid petrolatum possesses any advantage over aqueous solutions containing dextrose or sodium chloride. We have also questioned the generally held opinion that such antiseptics as menthol, eucalyptol, guaiacol or iodine, when dissolved in oil or in any other solute, can exert any important bactericidal action on bacteria or viruses developing in or beneath the nasal mucosa. Scientific proof, not personal opinion of the physician or patient, is necessary before we can rightly conclude that any of these exert a genuinely effective antibacterial or antiviral action. If only symptomatic anticongestive effects are aimed at by local medication, these can be as well secured by the use of aqueous solutions, thus avoiding the real dangers associated with the use of irritating oils. Statements that these intranasal preparations exert a "stimulating," "healing" or "bactericidal" effect should not be accepted until there is some objective evidence as to their validity. At present there is considerable evidence to the contrary. As Proetz³¹ has recently said in stressing the importance of the functional point of view in rhinology and the need for reexamination of therapeutic methods empirically employed, "It is likewise progress, though it seldom occurs to us to abandon old methods . . . when they have been discredited. Not to abandon them after they have been proved harmful is reprehensible."

No argument is necessary regarding the need for additional information about the therapy of infections of the upper part of the respiratory tract. Too much trust, however, has hitherto been placed on empiric treatment rather than controlled observation. As a result, the public has accepted this attitude, and self medication with nasal oils is widespread. It is not likely that this will be stopped until the medical profession takes the leadership in the educational campaign to eliminate the practice.

27. Healy, C. A.: Local Medication of the Upper Respiratory Tract, *J. A. M. A.* **107**: 1887-1889 (Dec. 5) 1936.

28. Proetz, A. W.: Effects of Certain Drugs on Living Nasal Ciliated Epithelium, *Ann. Otol., Rhin. & Laryng.* **42**: 450-463 (June) 1934.

29. Lierle, D. M., and Moore, P. M.: Effects of Certain Drugs on Ciliary Activity of the Mucosa of the Upper Respiratory Tract, *Arch. Otolaryng.* **19**: 55-65 (Jan.) 1934.

30. Fenton, R. A., and Larsell, Olof: An Experimental and Clinical Study of Histocytes in Acute and Chronic Inflammation of the Accessory Sinuses, *Laryngoscope* **43**: 233-241 (April) 1933.

31. Proetz, A. W.: Functional Point of View in Rhinology, *J. A. M. A.* **115**: 421-422 (Aug. 10) 1940.

23. Pinkerton, Henry: Oils and Fats: Their Entrance into and Fate in the Lungs of Infants and Children—A Clinical and Pathologic Report, *Am. J. Dis. Child.* **33**: 259-285 (Feb.) 1927.

24. Ikeda, Kano: Oil Aspiration Pneumonia (Lipoid Pneumonia), *Am. J. Dis. Child.* **49**: 985-1006 (April) 1935.

25. Monfort, J. A.: Lipoid Pneumonia, *M. Times* **67**: 320-325 (July) 1939.

26. Goodwin, T. C.: Lipoid Cell Pneumonia, *Am. J. Dis. Child.* **48**: 309-326 (Aug.) 1934.

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SATURDAY, DECEMBER 21, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

VIRUS STUDIES IN A NEW RESPIRATORY INFECTION

Many reports have appeared recently concerning an acute infectious disease of the respiratory tract in man, associated with unusual pathologic changes in the lungs. Sporadic cases as well as minor epidemics have been described occurring in various parts of the United States and abroad (England, France, Hawaii, Spain). The disease has been described under a variety of names, such as acute influenza pneumonitis (Bowen), acute pneumonitis (Allen), atypical pneumonia (Cass), acute interstitial pneumonitis (Smiley and others), bronchopneumonia (Miller and Hayes), atypical bronchopneumonia (Murray), circumscribed pneumonia and disseminated focal pneumonia. All these terms are too restrictive, since they describe pulmonary changes observed only in the more severe cases. The majority of the cases do not present these changes. Furthermore,

the terms fail to throw any light on the etiology of the infection. The disease differs from the familiar forms of lobar pneumonia caused by pneumococci and from bronchopneumonia caused by the hemolytic streptococcus, staphylococcus, *Pasteurella tularensis* and the forms accompanying acute infectious diseases of infancy and childhood.

Reimann¹ in 1938 described a series of 8 cases of an unusual, uniform, severe infection of the respiratory tract. The disease occurred in adults and began as a mild infection. This was followed by severe, diffuse atypical pneumonia and in the 2 fatal cases by symptoms of encephalitis. Dyspnea, cyanosis, cough without sputum, drowsiness and profuse sweating were the chief characteristics. Blood cultures remained sterile, and agglutinins for other bacillary diseases were absent. Kneeland and Smetana² reported 52 cases of atypical bronchopneumonia observed within the past two years at the Presbyterian Hospital, New York. The course of the infection was characterized by an insidious onset, a normal or only slightly elevated leukocyte count early in the disease, a sputum entirely comparable from a bacteriologic standpoint to that of healthy persons. The pulmonary consolidation was incomplete and tended to be migratory. Most of the cases were mild. The more severe cases presented a prolonged course, a tendency to relapse, cyanosis with obstructed breathing and leukocytosis late in the disease. Sulfapyridine had no antipyretic effect nor any effect on the course of the disease. The microscopic features of the pneumonia in the 1 fatal case were likewise unusual and were characterized by a mononuclear cell exudate and an acute pulmonary vasculitis.

There is abundant evidence to show that the disease is readily transmissible. Most of the reports refer to the occurrence of the disease among college students or in garrisoned troops. Miller and Hayes³ reported a small epidemic at the University of Oregon. Smiley, Showacre, Lee and Ferris⁴ reported a series of 86 cases occurring in a fifteen month period among the students at the Cornell University, while Maxfield⁵ reported a similar epidemic involving 63 cases of "atypical leukopenia pneumonia" seen at the Baylor Hospital, Dallas, Texas. Longcope⁶ points out that more than half of the 32 cases of this particular variety of pulmonary disease observed by him at the Johns Hopkins Hospital occurred during October, November and December, whereas pneumococcal pneumonia is most prevalent in Baltimore from December to May, a period

1. Reimann, H. A.: An Acute Infection of the Respiratory Tract with Atypical Pneumonia, *J. A. M. A.* **111**: 2377 (Dec. 24) 1938.
2. Kneeland, Y., Jr., and Smetana, H. F.: Current Bronchopneumonia of Unusual Character and Undetermined Etiology, *Bull. Johns Hopkins Hosp.* **67**: 229 (Oct.) 1940.
3. Miller, F. N., and Hayes, Marian G.: Bronchopneumonia of Mild Severity at the University of Oregon, *Northwest Med.* **38**: 12 (Jan.) 1939.
4. Smiley, D. F.; Showacre, E. C.; Lee, W. F., and Ferris, H. W.: Acute Interstitial Pneumonitis, *J. A. M. A.* **112**: 1901 (May 13) 1939.
5. Maxfield, J. R.: Atypical Pneumonia with Leukopenia, *Texas State J. Med.* **35**: 340 (Sept.) 1939.
6. Longcope, W. T.: Bronchopneumonia of Unknown Etiology, *Bull. Johns Hopkins Hosp.* **67**: 268 (Oct.) 1940.

during which only 8 of his 32 cases were encountered. The onset of the disease was similar in most of the cases, but the subsequent course varied greatly from a mild infection to one which was extremely grave or fatal. There was a moderate leukopenia in the beginning, the leukocytes rising in the later stage, seldom, however, higher than 13,000 and without a corresponding increase in the polymorphonuclear neutrophilic leukocytes. Frequently repeated blood cultures were negative, as were agglutinin reactions for *Pasteurella tularensis*, *Brucella abortus* and *Salmonella suipestifer*. Among the features which distinguish this infection as a disease entity Longcope points out the onset with high fever, headache, sweating, rasping, nonproductive cough that may become paroxysmal, the meager physical signs of consolidation of the lungs with spotty or dense shadows in the roentgenograms, the normal or slightly elevated leukocyte count and the infrequency of chill, pain in the chest and rusty sputum. The persistence of signs and symptoms for seven to fourteen days even in the mild cases and the prolonged course lasting three weeks or more in the severest infections form a striking feature. The disease presents many features which in Longcope's opinion suggest that it might be caused by a filtrable virus. These are its contagiousness, the long incubation period, the inability to demonstrate by culture of the sputum or of blood or by agglutination reactions that it is associated with any known pathogenic bacteria, and, finally, the peculiarity of the pathologic changes consisting of a mononuclear cell exudate into the pulmonary alveoli. Reimann and Havens⁷ describe an outbreak of an epidemic disease of the respiratory tract which occurred in Philadelphia in 1939. Of a group of 813 persons in the personnel of the Jefferson Medical College and Hospital 50 per cent were ill. Eighty-eight per cent of the patients were ill with nasopharyngolaryngitis, 6 per cent had tracheobronchitis and 6 per cent had tracheobronchopneumonia. The disease resembled epidemic influenza in many respects but was caused by a different agent. These authors call attention to the fact that, from the standpoint of public health, mild infections are all potentially dangerous. They may be the precursors of an outbreak of a more serious disease of the respiratory tract caused by the invasion of bacteria like that which occurred in 1918-1919 after influenza. Reimann believes that the failure to isolate a virus of these cases was probably due to the delay before attempts were made or to the weak pathogenicity of the virus for the species of animals which were inoculated. With only 2 patients of his first series¹ attempts were made to obtain a virus as early as the fourth day of illness. From both patients Dr. Stokes⁸ and Dr. Francis obtained an unusual virus from the nasopharyngeal washings of one and from the blood

of the other. It was equally virulent for mice and caused pneumonia and encephalitis about two weeks after inoculation. Unfortunately, however, the agent was lost before serologic tests could be done. Consequently evidence was not obtained regarding any etiologic relationship. Now Weir and Horsfall⁹ report unsuccessful attempts to infect a variety of animals such as ferrets, mice, guinea pigs, rabbits, monkeys, opossums, skunks, woodchucks, voles, deer mice and Syrian hamsters by intranasal inoculation with throat washings from a number of clinically typical cases. They took the infectious material to Kingston, Jamaica, in order to attempt to transmit the infection to the wild mongoose. The abundance of this animal in some of the Caribbean islands and the resemblance to the ferret were the chief reasons for this choice. They have succeeded in recovering a virus capable of producing pulmonary consolidation in this animal. The virus was filtrable through Berkefeld V and N candles, was not inactivated by glycerin or by freezing and drying in vacuum, and was propagated for at least thirty serial passages on the chorio-allantoic membrane of the developing chick embryo. Normal mongooses placed in contact with infected mongooses developed pulmonary consolidation. The virus was neutralized by the serum of mongooses convalescent from the infection but was not neutralized by normal mongoose serum. Serum of human beings convalescent from acute pneumonitis also neutralizes the virus, but serum obtained from the same persons during the acute phase of the disease failed to do so. The authors state that this virus is the cause of acute pneumonitis in human beings.

PULMONARY EMBOLISM IN MEDICAL PATIENTS

In the practice of surgery, pulmonary embolism has long been recognized as a frequent and important complication. Strangely, in the practice of internal medicine and in general medical practice this condition has been long neglected. Dr. Paul Dudley White,¹ of Boston, has recently reviewed twenty years of personal experience with pulmonary embolism and heart disease. The frequency of failure to recognize pulmonary embolism stresses the importance of the condition in simulating or complicating heart disease. From 1930 to 1940 he made the diagnosis of pulmonary embolism in his own practice seven times more often than in the ten year period from 1920 to 1930, though there was no essential difference either in the type of practice or in the numbers of new and old patients seen. As a matter of fact, even in the second decade the condition was largely overlooked during the first half; two thirds of the cases were seen during the last three of the total twenty

7. Reimann, H. A., and Havens, W. P. An Epidemic Disease of the Respiratory Tract, *Arch. Int. Med.* 65: 138 (Jan.) 1940.

8. Stokes, J., Kenney, A. S., and Shaw, Dorothy R.: A New Filtrable Agent Associated with Respiratory Infections, *Tr. & Stud., Coll. Physicians Philadelphia* 6: 329 (Feb.) 1939.

9. Weir, J. M., and Horsfall, F. L.: The Recovery from Patients with Acute Pneumonitis of a Virus Causing Pneumonia in the Mongoose, *J. Exper. Med.* 72: 595 (Nov.) 1940.

1. White, P. D.: Pulmonary Embolism and Heart Disease: A Review of Twenty Years of Personal Experience, *Am. J. M. Sc.* 200: 577 (Nov.) 1940.

years. Confirmation of the diagnosis was established by undoubted clinical or necroscopic evidence. Analysis of this experience and of the postmortem reports at the Massachusetts General Hospital indicates that there has not been an abrupt increase in pulmonary embolism and infarction but that the major part at least of the supposed increase was due to greater search for and better recognition of the condition. Erroneous clinical diagnoses of bronchial or atypical lobar pneumonia, of congestive heart failure (with pulmonary edema), and even of coronary thrombosis (in a few cases) have been responsible for some of the errors of omission.

Pulmonary embolism may simulate heart disease (coronary thrombosis or congestive failure) but more often it complicates heart disease, especially mitral stenosis or congestive heart failure from any cause. Peripheral venous thrombosis is clinically evident in a minority of the cases and even concealed at necropsy in many cases unless the veins are actually explored. In some 70 per cent of the medical cases with pulmonary embolism and infarction seen post mortem, venous thrombosis, which gave little or no clinical evidence of its presence, was present in the deep veins of the legs. Sixty per cent of all cases of pulmonary embolism and infarction are in "medical" patients (half with heart disease and half without).² Of course, in many a case the large dilated heart allows an intracardiac thrombus in the right heart chambers to be the source of pulmonary embolism, but this actually seems to be a relatively uncommon site of origin.

Clues to the diagnosis of obscure pulmonary embolism are presented by White as follows: (1) the occurrence of unexplained fever, leukocytosis, tachycardia, faintness, prostration, dyspnea, asthma or even jaundice (from hemolysis of a large infarct plus an engorged liver), especially in a patient with heart disease (and particularly in the presence of mitral stenosis or heart failure); (2) the finding of lung signs (rales or consolidation) not adequately explained by either congestive heart failure or pulmonary infection; (3) the periodic recurrence at short intervals of episodes that individually might be mistaken for acute coronary occlusion but which in series are much more likely to mean repeated pulmonary embolism; (4) the inexplicable lack of response of a case of congestive heart failure to therapy which seemingly should be adequate (ruling out other factors such as infection, infarction elsewhere than in the lungs and thyrotoxicosis), and (5) in a few cases the characteristic electrocardiogram of the acute cor pulmonale (prominent S waves in lead 1, low, flat or even inverted T waves in lead 2, prominent Q waves and inverted T waves in lead 3 and low, flat or inverted T waves in lead 4) when the right ventricle is dilated by massive embolism (not therefore in the

majority of cases of pulmonary embolism) and simulating at first glance the electrocardiogram of acute coronary thrombosis with basal infarction.

Pulmonary embolism always demands a careful search for peripheral venous thrombosis and heart disease. Its detection explains obscure signs and symptoms, refractoriness to treatment and periodic episodes of fever, tachycardia or collapse. Its presence reveals the folly of forcing unnecessarily vigorous, perhaps toxic, therapy for congestive heart failure and points to the possible help, even life saving in rare cases, to be derived from ligation of a peripheral vein.

The chief lesson to be learned from studies of important diagnostic errors of omission is the necessity to remember all the possible common causes of any given combination of symptoms and signs. Pulmonary embolism is a common cause of primary or complicating intrathoracic disease.

Current Comment

MONGOLIAN SPOTS AND NEGRO HEREDITY

In a recent discussion¹ of a case involving rape the question of Mongolian spots as an indication of Negro inheritance received special attention. The so-called Mongolian spot is a curious manifestation of pigmentation which consists of one or more bluish dark spots that appear at birth in the sacral, lumbar and gluteal regions. These spots resemble the black and blue marks on the skin after a contusion, and, according to Dr. Carleton Simon, consulting criminologist to the Association of Chiefs of Police of the State of New York, one of the consultants in the case in question, they are more distinct the first two weeks, becoming fainter and disappearing in from two months to two years. Ninety per cent of all Japanese infants have them, and they are common also among infants of the Javanese, Malays, Chinese, natives of Greenland and tribes of the American Indian. In the Negro the Mongolian spot is rarely absent, several of the spots usually being present in the same individual. They have also been found in a few instances among Russians and the darker Mediterranean white races. Dr. Hooton, writing on the same subject, points out that the presence of Mongoloid spots is suggestive but not definitive of Negro blood and occurs also in infancy in many of the darker pigmented races. Parallel discussions of other features which have been considered as indicative of Negro blood, including physical characteristics such as increased pigment in the eyes and nails and blood tests, lead to the conclusion that there is as yet no known scientific test that will identify the racial background of a person whose blood contains so many and so dilute racial strains as to make his racial origins doubtful. Furthermore, the mathematical computation that in twenty generations every individual is the lineal descendant of

2. Hampton, A. O., and Castleman, B.: Correlation of Postmortem Chest Teleroentgenograms with Autopsy Findings, with Special Reference to Pulmonary Embolism and Infarction, *Am. J. Roentgenol.* 43: 305 (March) 1940.

1. Bulletin, Bureau of Criminal Investigation, New York State Police, Albany 5: 6 (April) 1940.

more than a million forebears symbolizes the complicated nature of the subject. In any event, the presence of Mongolian spots alone cannot be considered to prove the presence of Negro blood in any immediate sense.

OIL ASPIRATION PNEUMONIA

Oil pneumonia, known also as lipid or lipoid pneumonia, in adults, due to liquid petrolatum, has been occurring increasingly in recent years. Errors in diagnosis may occur whereby the condition is overlooked, so that it is detected only at necropsy, if at all. Freiman and his associates¹ have shown that the aspiration of liquid petrolatum is facilitated by the fact that it is a bland drug, nonirritant to the pharyngeal mucosa and exciting no reflex inhibition. When once aspirated, gravity and inspiratory suction seem to control its disposition in the lungs. This is indicated by the fact that the lower right and left lobes are preponderantly affected. Forty-seven mostly debilitated recumbent and dysphagic patients who were suffering from some incurable disease such as carcinoma or arteriosclerosis, with an average age level of 61.8 years, had habitually used liquid petrolatum in relatively large quantities. Forty-one of these were studied at necropsy. The microscopic examination of pulmonary tissue indicates two stages in the evolution of the disease, a prompt macrophagic reaction followed by a slower process of fibrous proliferation of interstitial tissue, which eventually prevails. As fibrosis increases, cellularity diminishes. Finally there remains only a mass of hyalinized fibrous tissue with entrapped oil, a true paraffinoma. The difficulty of clinical diagnosis is increased by the absence of specific symptoms and signs. Symptoms such as cough, blood-streaked sputum, if present, pain in the chest and intercurrent fever are those associated with other forms of chronic pulmonitis. Malignant growths present elsewhere than in the lung may lead to a wrong interpretation of pulmonary shadows as metastatic in origin; but here the failure of pulmonary infiltration to increase in size over a period of months after cessation of intake of oil is strong evidence against tumoral metastasis. Laboratory data are only occasionally helpful, as the leukocyte count and the erythrocyte sedimentation rate are not affected by liquid petrolatum by itself. On the other hand, the presence in the sputum of oil globules is diagnostically valuable, if liquid petrolatum can be identified chemically or by differential staining. However, diagnosis is significantly aided by roentgenoscopy. In the early stages the markings in the lower lung fields are exaggerated. As the lesions progress, linear and nodular infiltrations develop until finally areas of consolidation are formed which are always situated at one or both pulmonary bases and which lie close to the cardiac shadow that extends from the hilus to the diaphragm. Serial roentgenograms may show no change for years other than progressive fibrosis, yet the persistence of pulmonary shadows in a patient with dysphagia receiving liquid

petrolatum justifies the diagnosis of oil aspiration pneumonia. The essential features of oil pneumonia are dysphagia, a long history of intake of oil, roentgenographic demonstration of persistent, unchanging consolidations characteristically situated in the mesial portions of the bases of both lungs and complete absence of clinical evidence of pulmonary disease; but they are rarely all present. The difficulty of correct diagnosis may be illustrated by a case cited from the authors' own experience in which oil pneumonia developed during two and one-half years of hospitalization of a patient suffering with degenerative cerebellar disease, pseudobulbar palsy and dysphagia. The progress of the lesion was followed roentgenologically throughout the illness and yet the diagnosis was not established until it was too late to affect the outcome by the withdrawal of the oil. The presence of persistent pulmonary consolidations with disproportionately slight symptoms or of infiltrations which do not fit into any well established disease pattern should suggest oil pneumonia. The authors do not consider oil aspiration pneumonia a direct cause of death, unless in some extreme case, as one which fell within their experience, in which the pulmonary lesion was so extensive as to induce asphyxia. Usually the patient lives for an indefinite time and finally succumbs to his primary disease or to a secondary infection. However, purulent bronchiolitis and bronchitis, bronchiolectasis, occasionally bronchiectasis and recurring episodes of bronchopneumonia may be concomitant conditions over a considerable period. Though the use of liquid petrolatum is not necessarily productive of oil pneumonia even in the presence of some predisposing factor, it is not without potential danger. Its promiscuous use, especially by enfeebled or dysphagic persons, should be discouraged.

BODY WEIGHT AND CANCER INCIDENCE

Many external factors affect the incidence of cancer. Among those recently discussed are climate, exposure to the elements, especially sunlight, and geographic location.¹ Now Tannenbaum² presents experimental and statistical evidence on the relation of body weight to the development of cancer. In both animals and man individuals of average or less than average weight are not as likely to develop cancer as those who are overweight, he believes. This tentative conclusion requires careful checking, and the establishment and maintenance of weight levels with a view to the prevention of human cancer can as yet be considered only as an experimental procedure. In the light of the curiously large number of correlations between cancer and internal and external factors which are now receiving attention, it is necessary to weigh all the evidence carefully and not to accept the suggestions as established until unequivocal proof has been presented.

1. Freiman, D. G.; Engelberg, Hyman, and Merrit, W. H.: Oil Aspiration (Lipoid) Pneumonia in Adults: A Clinicopathologic Study of Forty-Seven Cases, *Arch. Int. Med.* 66:11 (July) 1940. Lipoid Pneumonia, editorial, *J. A. M. A.* 114:251 (Jan. 20) 1940.

1. Peller, Sigismund; Stephenson, C. S., and Souder, C. G.: Cancer and Its Relations to Climatic Conditions Acting During Childhood and Adolescence, *Am. J. Hyg.* 32:39 (July) 1940. Peller, Sigismund: Skin Irritation and Cancer in the U. S. Navy, *Am. J. M. Sc.* 104:326 (Sept.) 1937. Bechet, P. E.: Excessive Solar and Phototherapeutic Irradiation, *Arch. Dermat. & Syph.* 29:221 (Feb.) 1934. Craver, L. F.: Etiology of Cancer, *J. A. M. A.* 103:1820 (Dec. 7) 1935. Mountain, J. W., and Dorn, H. F.: Some Peculiarities in the Geography of Cancer, *ibid.* 112:2405 (Dec. 30) 1939.

2. Tannenbaum, Albert: Relationship of Body Weight to Cancer Incidence, *Arch. Path.* 30:509 (Aug.) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

CHANGES IN COMMITTEE CHAIRMANSHIPS OF DIVISION OF MEDICAL SCIENCES OF NATIONAL RESEARCH COUNCIL

In order to meet new and expanding requirements in the field of medical preparedness, the following changes in the chairmanships and organization of committees in the Division of Medical Sciences of the National Research Council have been announced by Dr. Lewis H. Weed, chairman of the Division of Medical Sciences:

Russell M. Wilder, Rochester, Minn., resigns as chairman of the Committee on Medicine (remains member of committee) to become chairman of the Committee on Food and Nutrition of the Division of Biology and Agriculture and of the Division of Medical Sciences.

O. H. Perry Pepper, Philadelphia, becomes chairman of the Committee on Medicine, resigned as chairman of the Subcommittee on Diagnosis and Therapeutics.

Hugh Morgan, Nashville, Tenn., becomes vice chairman of the Committee on Medicine.

James McLester, Birmingham, Ala., becomes chairman of the Subcommittee on Medical Nutrition.

Warfield T. Longcope, Baltimore, becomes chairman of the Subcommittee on Diagnosis and Therapeutics.

Henry Meleney, Nashville, Tenn., becomes chairman of the Subcommittee on Tropical Diseases vice Wilbur A. Sawyer (resigning because of duties abroad).

The complete organization was described in THE JOURNAL, November 9, page 1640.

A COMMITTEE ON FOOD AND NUTRITION TO ADVISE GOVERNMENT

The National Research Council announces the appointment of a Committee on Food and Nutrition to advise the federal government on nutritional aspects of national defense. This committee, appointed at the request of Miss Harriet Elliott, head of the Consumer Division of the National Defense Advisory Commission, will concern itself with improving the nutrition of the general population. A separate National Research Council subcommittee is already advising the Army and Navy on nutrition for these services. Several members of this subcommittee are also members of the new Committee on Food and Nutrition.

Dr. Russell M. Wilder, of the Mayo Clinic, Rochester, Minn., is chairman of the new committee. Serving with him as advisers to the government in planning its program of national nutrition for defense are specialists from agriculture, industry and science dealing with food and nutrition.

Representing the food processing industry are Mr. Cullen Thomas, executive of General Mills Corporation, Minneapolis, and Dr. Samuel C. Prescott, dean of science, Massachusetts Institute of Technology, and member of the Institute of Food Technologists. For advice on problems of food production and distribution the committee includes Dr. John N. Black, professor

of agricultural economics at Harvard University. Dr. F. G. Boudreau, now executive director of the Milbank Memorial Fund but formerly head of the League of Nations technical committee on nutrition, and Dr. Joseph S. Davis, professor of economic research and director of the Food Research Institute, Stanford University, will contribute their knowledge of world food problems, as will Dr. John B. Youmans, associate professor of medicine, Vanderbilt University, who is now studying the food problems of both occupied and unoccupied France for the Rockefeller Foundation.

Advice on translating nutritional science into menus and diet lists for the welfare of the family will come to the housewife from such experts as Dr. Icie Macy Hoobler, director of research laboratory, Children's Fund of Michigan, Detroit; Dr. Helen S. Mitchell, research professor of nutrition, Massachusetts State College, Amherst, and Dr. Lydia J. Roberts, chairman of the Department of Home Economics, University of Chicago.

Specialists in certain phases of nutrition are serving on the committee. In the vitamin field a group is made up of Dr. R. R. Williams, chemical director, Bell Telephone Laboratories, who first isolated and later synthesized thiamine; Dr. George R. Cowgill, associate professor of physiologic chemistry, Yale University; Dr. C. A. Elvehjem, professor of agricultural chemistry, University of Wisconsin, and Dr. Norman Jolliffe, associate professor of medicine, New York University School of Medicine; Dr. Henry Borsook, professor of biochemistry, California Institute of Technology; Dr. Charles Glenn King, professor of chemistry, University of Pittsburgh, known for his isolation in pure form of vitamin C; Dr. Philip C. Jeans, professor of pediatrics, State University of Iowa, and Dr. W. C. Rose, professor of biochemistry, University of Illinois.

Broad as well as specialized knowledge of nutritional science will be contributed by Dr. James McLester, professor of medicine, University of Alabama, and Dr. L. A. Maynard, professor of animal nutrition and director, U. S. Plant, Soil and Nutrition Laboratory, Cornell University. Dr. McLester is chairman of the American Medical Association's Council on Foods and Nutrition and Dr. Maynard is secretary of the American Institute of Nutrition.

The committee recently held its first meeting in Washington. It gave consideration to the improvement of white flour, which is well known to be deficient in the B vitamins, necessary for health and morale, and in minerals. It will consider the possibilities of improving the quality of sugar, which likewise has been deprived of the vitamins and minerals contained in the material from which it is made—sugar cane and beets. Means will also be sought for improving the nutritional qualities of other staple foods, such as the edible fats.

It is the quality of the nation's food that is important in the present emergency, it was pointed out, whereas in the war of 1914-1918 the quantity of food was the

chief concern. It is for this reason that Miss Elliott asked for a committee of scientists to advise her, through Dr. M. L. Wilson, director of extension work, U. S. Department of Agriculture, how much of each important nutritional factor should be included in the national diet, and what things the public should be taught to eat. A national program of nutritional education is in planning, directed by Dr. Wilson.

One of the things to be taught, the committee decided at its first meeting, is that there is no detectable difference between the synthetic chemical vitamins and the natural ones. Ascorbic acid is just as good vitamin C, for example, as one gets from an orange.

Serving on the committee as liaison representatives from the American Red Cross and the United States government services will be a number of persons, several of them well known for their research in nutrition. Among those already appointed are Colonel Paul E. Howe, Dr. W. H. Sebrell, Commander Charles S. Stephenson, Dr. William DeKleine and Dr. Louise Stanley. The following authorities on nutrition have been asked to serve as advisers to Miss Elliott. They also will be asked to serve the committee as consultants: Prof. E. V. McCollum, Dr. John R. Murlin, Prof. Mary Swartz Rose and Prof. H. C. Sherman. Ex-officio members of the committee are Mr. M. L. Wilson, of the National Defense Nutrition Program, and Dr. Robert Griggs and Dr. Lewis H. Weed, chairmen, respectively, of the National Research Council's Division of Biology and Agriculture and Medical Sciences.

THE NATIONAL YOUTH ADMINISTRATION CONTRIBUTES TO THE NATIONAL HEALTH

The National Youth Administration has launched a nationwide health program to serve the needs of young workers who are employed on its out-of-school work program. This effort to afford young people the experience of practical health education in order to help strengthen the nation's vital defenses by building a strong and healthy population will be directed along three major lines:

1. A physical appraisal, by means of a technically competent health examination, of every youth assigned to an NYA job;
2. Correction of health defects through maximum utilization of community resources, through the use of supplementary medical and dental services provided where possible by the National Youth Administration and through developing in youth an interest in improving their health by their own personal efforts;
3. Improved technical advice and assistance with respect to all NYA efforts having a direct and immediate bearing on the health of youth workers, such as nutrition, sanitation, physical development and recreation.

At the September meeting of the Conference of State and Territorial Health Officers, Aubrey Williams, National Youth Administrator, outlined the purpose and scope of the out-of-school work program. Dr. Carl E. Rice, Surgeon, U. S. Public Health Service, assigned to the National Youth Administration, presented the general plans for the health program which is under his direction. The Committee on Hospital and Medical Care of this conference endorsed the proposed program in the following resolution:

WHEREAS, The health program to be initiated by the National Youth Administration is planned to promote the health and efficiency of its enrolled youths through the utilization of health

and medical facilities which already exist, or may be supplemented by the National Youth Administration; and

WHEREAS, The program as planned seeks the active cooperation of state and local health departments: be it

Resolved, That the Conference of State and Territorial Health Officers endorse the principles and purpose of the National Youth Administration's health program; and

That the Conference recommend that the state health department serve, when requested, as co-sponsor of such statewide National Youth Administration health projects.

In addition to extending health services to youth, the National Youth Administration will continue through its work program to improve and extend community health facilities. During the year ended June 30, 1940, the record of accomplishment includes the production of over eight million articles of hospital supplies for public institutions, the construction of nine new hospitals and repairs and improvement to sixty-two others, the construction of forty other new buildings concerned with various health activities, and repairs and improvements on one hundred and thirty-one others. In addition, many young persons received work experience in a variety of hospital functions as ward attendants, laboratory assistants and kitchen and laundry workers.

The work program aims to acquaint young workers with modern production methods and prepares them for present employment conditions. Young men and young women gain practical work experience through employment on projects which produce useful articles, facilities and services for public agencies. Work experience in welding, sheet metal work, radio construction, automobile mechanics, wood working, sewing, book repair and office work is productive of articles for city and county departments and offices as police, welfare, health, education and sanitation.

As most of the National Youth Administration's work with unemployed young persons has a close relationship to the broad needs of defense, it has been designated as one of the National Defense agencies.

It is estimated that approximately five hundred thousand young persons out of school between the ages of 17 and 24 inclusive will be employed on the work program during the fiscal year. About 50 per cent of the persons so employed are young men. The average period of employment is less than one year. All of them come from families in the lower economic brackets. Increased employability and work productivity are important at all times, and especially at present.

One important aspect of the NYA work program, the operation of both resident and nonresident projects, influences the character of the health program. About fifty thousand young persons are employed on resident projects, where they live at the job site under NYA supervision twenty-four hours each day. In these resident projects the National Youth Administration must assume responsibility for the medical care of a comparatively small group of young persons. This is not true for the much larger group of employed young persons. The NYA health program is not a medical care program, as responsibility for providing medical care for intercurrent illnesses of the employed young persons will remain with the family or community except for the small group mentioned.

The health examination for all young persons will be made largely by designated practicing physicians. This examination follows a standard national form and includes provision for necessary smallpox vaccination, for routine serologic blood test and urinalysis, and for a routine chest roentgenogram or a routine tuberculin test followed by chest roentgenograms for positive

reactors. Everything possible is being done to assure the health education value of the examination. The examination is not regarded as a hurdle for young persons desiring to enter into NYA employment. The main purposes for giving the examination are to:

- (a) facilitate proper work assignment;
- (b) assist in the guidance of young persons in physical development and health education activities;
- (c) discover health conditions that need attention.

Naturally, young persons with communicable disease, severe heart lesions or mental abnormality must be excluded. It is not intended to exclude any youth from NYA employment because of physical limitations and consequent limitations in work capacity, unless such employment will endanger the life of the individual youth or will endanger the health and safety of other young persons.

The rehabilitative effort is aimed at the correction of actual and potential health hazards and those conditions which may not be health hazards but may reduce the employment possibilities and well-being of the youth. A great part of this effort will be through influencing the young people to make their own arrangements with physicians and dentists, using a portion of their NYA wage in payment for services. This will require considerable skilful counseling with the youth concerned on the part of NYA personnel. Success will depend also on the degree of consideration and cooperation given this effort by practicing physicians and dentists. In some areas, much of the necessary follow-up work can be secured through existing community agencies if such is necessary. Such facilities, however, are usually overburdened in taking care of sick people and are not particularly desirable places to send apparently healthy persons, either for examination or for corrective work.

The National Youth Administration will establish its own facilities in some regions in connection with larger projects, utilizing the services of practicing physicians and dentists in the community on a part-time basis. Local economic conditions and the presence or absence of going health facilities will indicate the necessity for NYA supplementation.

The health of NYA employees will also be approached through activities in the field of nutrition, health information, physical training and recreation.

Each state health program will be directed by a physician of outstanding professional competence who will serve on the staff of the state administrator on a part-time basis, as health consultant, to give technical supervision and direction to all NYA health efforts. Assisting him and employed on a full-time basis to direct the statewide health project is the state health supervisor. The supervisor is usually a nonmedical person selected from the fields of public health nursing or physical education or from administrative positions in public and private health associations. Statewide health projects in every state operate in collaboration with state public health departments, which in most cases are giving material assistance in the supervision and operation of NYA health activities.

One of the main jobs of the health consultant will be to assure the wise expenditure of NYA funds. Another function will be concerned with utilizing existing health facilities to the fullest extent and securing the cooperation of practicing physicians and dentists. He will also be responsible for reviewing and making recommendations concerning medical services rendered in resident centers by physicians and dentists employed on a part-time or full-time basis.

The cooperation of the medical and dental professions will be necessary to enable the plan to succeed. As the various NYA state administrators approach officials and committees of state medical and dental societies, it is hoped that the representatives of the two professions will keep in mind that the NYA health program is primarily a practical health education effort aimed at influencing the future health practices of a group of young out-of-school unemployed persons, who will usually remain in NYA employment for only a short period.

The method of attempting to accomplish this purpose will be through imparting health information, acquainting and introducing the young people to the public and private health facilities available in their own state and community, and finally by exposing them to rehabilitative health services obtainable from the private practitioner either on the youth's own initiative or through NYA supplementation as may be indicated.

NEW CORPS AREA SURGEON

Col. Joseph E. Bastion, M. C., U. S. Army, has been announced as Corps Area Surgeon of the Sixth Corps Area with station at Chicago, to succeed Col. Paul W. Gibson, M. C., U. S. Army.

COLONEL SPRUIT ASSIGNED TO GENERAL HEADQUARTERS

Lieut. Col. Charles B. Spruit, Medical Corps, U. S. Army, who has been chief of the medical division of national headquarters, Selective Service System, since last August, has been assigned to the General Staff in the War Department and will be on duty at General Headquarters, Army War College, Washington, D. C.

NEW GENERAL HOSPITAL IN THE NORTHWEST

The War Department has announced that authority has been given for the construction of a 750 bed cantonment-type general hospital at Vancouver Barracks, Washington, to serve the military personnel in the Northwest states area. This hospital will be used in connection with existing facilities at the station hospital already at Vancouver Barracks and it is expected to be ready for occupancy early in 1941.

FORT DEVENS OFFICERS FORM SCIENTIFIC GROUP

The medical officers at Fort Devens, Mass., have formed the Society of the Medical Department Officers and have been conducting scientific meetings at the station hospital on Tuesday evenings. Beginning October 8, with an address by Lieut. A. W. Bennett on "Peptic Ulcer," the speakers have included Lieut. Miles Kelly on bronchiectasis, Lieut. Charles C. Verstandig on "Roentgen Therapy in Pneumonia," Dr. E. A. Adams, Fitchburg, Mass., "Treatment of Appendicitis," Dr. Thomas H. Ham, Boston, "Hemorrhagic Diseases and Treatment," Dr. Harry Blotner, Boston, "Diabetes Mellitus," and, December 10, Dr. Atanley J. G. Nowak, Boston, "Shock." Col. H. P. Carter has been chosen president of this group and Lieutenant Verstandig, secretary.

MEDICAL CORPS ORDERS

The following orders have recently been issued to officers of the Medical Corps of the U. S. Army:

Col. Hew B. McMurdo, from the Philippine Department to be Instructor in the Medical Corps, 33d National Guard Division, Chicago area.
Col. Joseph Casper, Winthrop, Mass., retired October 31 on account of disability incident to the service.

Capt. Francis F. Viglione, from Madison Barracks, N. Y., to the Puerto Rican Department, leaving New York November 27.

Lieut-Col. Leonard W. Hassett, from Philippine Department to Fort Slocum, N. Y.

Lieut-Col. Lucius K. Patterson, from Panama Canal Department to Fort Riley, Kan.

Capt. Stephen C. Sitter and Capt. Edwin S. Kagy, from Washington, D. C., to the Philippine Department, sailing December 28.

Capt. Hubert T. Marshall, from Hawaiian Department to New York General Depot, New York Port of Embarkation, Brooklyn.

Capt. Edwin M. Goyette, from Carlisle Barracks, Pa., to Panama Canal Department, sailing January 18.

Capt. George F. Peer, from Panama Canal Department to New York Port of Embarkation, Brooklyn.

ARMY RESERVE OFFICERS

WAR DEPARTMENT

The following additional medical reserve officers had been ordered to extended active duty by order of the War Department, Washington, D. C., up to December 6:

ADAMO, Frank Scozzari, Lieut. Col., Tampa, Fla.
ALFORD, Thomas Dale, 1st Lieut., Little Rock, Ark.
BAUMHAUER, Charles Andrew, 1st Lieut., Whistler, Ala.
COSBY, Oswald Whitney, Captain, Baton Rouge, La.
CRAIN, Alfred Penn., Jr., 1st Lieut., Shreveport, La.
DAMROW, Harold Byran, Captain, Bristol, Va.
DAVIS, Richard Fleming, 1st Lieut., Batavia, N. Y.

DIODATI, Anthony Dominic, 1st Lieut., Philadelphia.
ELLIS, Herbert B., 1st Lieut., Raton, N. M.
HELLMAN, Jack M., 1st Lieut., Chicago.
LANDER, Herman Boris, 1st Lieut., Chicago.
McCLARY, George Robin, 1st Lieut., Miami, Fla.
MORRISSEY, Paul Gunkle, Jr., 1st Lieut., Nashville, Tenn.
POHL, Robert Leo, 1st Lieut., Spokane, Wash.
RAPALSKI, Adam Jozef, 1st Lieut., Nutley, N. J.
SHUTKIN, Manfred Ned, 1st Lieut., Milwaukee.
SPALDING, Joseph John, 1st Lieut., Indianapolis.
STERN, Robert Leo, 1st Lieut., Los Angeles.
STEWART, Magnus Jackson, Captain, Loveland, Col.
THAYER, Kent H., 1st Lieut., Phoenix, Ariz.
WINSOR, Carlton Webb, Captain, Detroit.

FIRST CORPS AREA

The following medical reserve corps officers had been ordered to extended active duty with the regular army by First Corps Area orders up to November 29. The First Corps Area comprises the states of Maine, Vermont, New Hampshire, Rhode Island, Massachusetts and Connecticut.

ARCHAMBEAULT, Armand C., Captain, Barre, Vt.
BLACK, Harry, 1st Lieut., Lowell, Mass.
CENTRONE, Patrick A., 1st Lieut., Middletown, Conn.
CINCOTTI, John J., 1st Lieut., Belmont, Mass.
CRAPOLICHIO, Dante V., 1st Lieut., Worcester, Mass.
CUMMINGS, Vincent P., 1st Lieut., North Adams, Mass.
DIPIPPO, Palmiro, 1st Lieut., Providence, R. I.
FRANK, Israel R., Captain, Jamaica Plain, Mass.

LANOU, William W., 1st Lieut., Pittsfield, Mass.
LEAVITT, Benjamin, 1st Lieut., Fall River, Mass.
LEVY, William S., 1st Lieut., Woonsocket, R. I.
MAHER, Joseph P., 1st Lieut., Milton, Mass.
McIVER, Frederick D., 1st Lieut., Orleans, Vt.
NATHANS, Samuel, 1st Lieut., Hope Valley, R. I.
PEKALA, Joseph G., Captain, Northampton, Mass.
QUIGLEY, George E., 1st Lieut., Newton, Mass.
RISMAN, Joseph, 1st Lieut., Lynn, Mass.
SCHILLER, Irving W., 1st Lieut., Dorchester, Mass.
SHAPIRO, Phillip, 1st Lieut., Northampton, Mass.
SHAPIRO, Robert, 1st Lieut., Roxbury, Mass.
TIEDE, Joseph W., Major, Dedham, Mass.
WEINSTEIN, Barnett, 1st Lieut., Peabody, Mass.
WILSON, William J., Jr., 1st Lieut., Derry, N. H.
YORK, Charles L., Jr., 1st Lieut., Plymouth, N. H.

SECOND CORPS AREA

The following additional medical reserve corps officers had been ordered to active duty by the Commanding General, Second Corps Area, up to December 6. The Second Corps Area comprises the states of New York, New Jersey and Delaware.

GESSNER, Gerard R., 1st Lieut., Highland Park, N. J., 3d Military Area.

HANFLING, Seymour L., 1st Lieut., Jamaica, N. Y., 2d Military Area.
LEVINE, David, 1st Lieut., New York, 2d Military Area.
MICELI, John N., 1st Lieut., Brooklyn, 2d Military Area.
MORAN, John F., 1st Lieut., Lambertville, N. J., 3d Military Area.
PERLMUTTER, Irving K., 1st Lieut., Newark, N. J., 3d Military Area.
ROBERTS, Arthur J., 1st Lieut., New York, 2d Military Area.
ROSS, Selig J., 1st Lieut., Allendale, N. Y., 2d Military Area.
SHULMAN, Bernard H., 1st Lieut., Secaucus, N. J., 3d Military Area.

THIRD CORPS AREA

The following medical reserve corps officers had been ordered to extended active duty by the commanding general of the Third Corps Area up to December 6. The Third Corps Area comprises the states of Pennsylvania, Virginia, District of Columbia and Maryland.

CLARK, Walter Scott, Jr., 1st Lieut., Burgettstown, Pa.
DEVLIN, Laurence Patrick, Captain, Philadelphia.
DONLEY, Donald, Captain, Sharon, Pa.
NATHANSON, Leon Irving, 1st Lieut., Washington, D. C.
SHAPIRO, Abraham Albert, 1st Lieut., Baltimore.
STASKIEL, Louis Julius, Jr., 1st Lieut., Glen Lyon, Pa.

FOURTH CORPS AREA

The following additional medical reserve corps officers had been ordered to active duty by Fourth Corps Area order up to December 6. The Fourth Corps Area comprises the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana.

BLACK, Paul A. L., 1st Lieut., Wilmington, N. C.
BROWN, George C., Jr., 1st Lieut., Walterboro, S. C.
CHAMBERS, Wallace L., 1st Lieut., Pickens, Miss.
DAVIS, William B., 1st Lieut., College Park, Ga.
deCAMP, Allen L., 1st Lieut., Fayetteville, N. C.
DRISCOLL, Robert H., Captain, Newberry, S. C.
EDMONDSON, Hansel E., Captain, Edwards, Miss.
FISHER, Roy A., Jr., 1st Lieut., Knoxville, Tenn.
FOURRIER, Daniel J., 1st Lieut., Baton Rouge, La.
HALL, James B., 1st Lieut., Gainesboro, Tenn.
HUSKEY, Aubrey L., Captain, Atlanta, Ga.
JORDAN, William K., 1st Lieut., Milledgeville, Ga.
KILGH, George F., Jr., 1st Lieut., Atlanta, Ga.
McCOIN, Joseph, 1st Lieut., Lafollette, Tenn.
McGUFFIN, William C., 1st Lieut., Asheville, N. C.

MOLE, John W., Captain, Brunson, S. C.
MURPHREE, Walter E., Captain, Gainesville, Fla.
NEILL, Francis K., 1st Lieut., Albany, Ga.
NEWMAN, Lucian, 1st Lieut., Dadeville, Ala.
PROUET, Prudence E., 1st Lieut., New Orleans.
PRUSA, Victor H., 1st Lieut., Banners Elk, N. C.
RALSTON, Raymond H., 1st Lieut., Lakeland, Fla.
SPEARMAN, Walter D., Captain, Social Circle, Ga.
STEM, William A., 1st Lieut., Chattanooga, Tenn.
TANNENBAUM, Abraham J., 1st Lieut., Greensboro, N. C.
TEMPLES, Leo G., 1st Lieut., Statesboro, Ga.
WILKES, Samuel M., 1st Lieut., Laurens, S. C.

Relieved from Duty or Orders Revoked

The following officers, previously reported, have been relieved from duty or the orders have been revoked:

ARNOLD, Laurie J., Jr., 1st Lieut., Lake City, Fla.
EVANS, Milton L., 1st Lieut., Memphis, Tenn.
FERRELL, Thomas J., 1st Lieut., Waycross, Ga.
McCORD, William M., 1st Lieut., New Orleans.
VOORHIES, Norton W., 1st Lieut., New Orleans.
WORK, Samuel D., Jr., 1st Lieut., Forsyth, Ga.

FIFTH CORPS AREA

The following additional medical reserve corps officers had been ordered to active duty by Fifth Corps Area order up to November 29. The Fifth Corps Area com-

prises the states of Ohio, West Virginia, Indiana and Kentucky.

BONETA y RIOS, Thomas Luis Eusebio, 1st Lieut., McKee, Ky.
VEIRS, Everett Raymond, Captain, Ashland, Ky.

SIXTH CORPS AREA

The following additional medical reserve corps officers had been ordered by Sixth Corps Area Order up to December 6 to extended active duty. The Sixth Corps Area comprises the states of Wisconsin, Michigan and Illinois.

BARAK, Herbert G., 1st Lieut., Dixon, Ill.
BASSUENER, Reynold O., Captain, Warrens, Wis.
CONKLIN, James O., 1st Lieut., Paris, Ill.
DRESNER, Milton H., 1st Lieut., Chicago.
DUNN, Max Martin, 1st Lieut., Chicago.
FLORETH, Nelson K., 1st Lieut., Litchfield, Ill.
GAUTSCH, Joseph A., 1st Lieut., Decatur, Ill.

HILL, George R., 1st Lieut., Fairfield, Ill.
HOLNITSKY, Samuel C., 1st Lieut., Chicago.
HRINKO, Stephen A., Captain, Detroit.
JOHNSON, Clarence E., 1st Lieut., Hillsdale, Mich.
KALLEN, Irvin A., 1st Lieut., Chicago.
KAPLAN, Louis G., 1st Lieut., Chicago.
LOOBY, WILLIAM E., 1st Lieut., Highland Park, Ill.
LUETH, Harold C., Captain, Evanston, Ill.
MALOW, Louis, 1st Lieut., Chicago.
McCORMICK, Donald W., 1st Lieut., Madison, Wis.
MIDDLETON, John W., 1st Lieut., Detroit.
PYZIK, Stanley W., 1st Lieut., Chicago.
RECK, Lawrence E., 1st Lieut., Peoria, Ill.
ROBINSON, Ralph D., 1st Lieut., Moberly, Mo.
ROCCO, Paul Carl, Captain, Chicago.

SEVENTH CORPS AREA

The following additional medical reserve corps officers had been ordered to extended active duty by Seventh Corps Area Order up to December 6. The Seventh Corps Area comprises the states of North Dakota, South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri and Arkansas.

ARMY, Frederick Phillip, 1st Lieut., Preston, Minn., Fort Snelling, Minn.
ATKINSON, George Stanford, 1st Lieut., White Earth, Minn., Fort Snelling, Minn.
BARTON, John Currer, Captain, Independence, Iowa, Fort Snelling, Minn.
COTTRELL, Wilson Philip, Major, Reed Springs, Mo., Fort Snelling, Minn.
ENGLISH, Wallace Davis, Captain, Cardwell, Mo., Fort Snelling, Minn.
GRAY, Herschel Frederick, 1st Lieut., Little Rock, Ark., Fort Snelling, Minn.
HAENTZCHEL, Lester Esaias, 1st Lieut., Fulton, Mo., Fort Snelling, Minn.
HANNA, Joe Tyntalinio, 1st Lieut., Omaha, Fort Crook, Neb.
HARRIS, Leon Dunham, 1st Lieut., Mobridge, S. D., Fort Crook, Neb.
HEIDRICK, Paul John, 1st Lieut., Lincoln, Neb., Fort Snelling, Minn.
HEPPERLEN, Harry Michael, Captain, Beatrice, Neb., Fort Snelling, Minn.
JOHNSON, Marvin Anthon, 1st Lieut., Plainview, Neb., Fort Snelling, Minn.
KLEYKAMP, Elmer August, Jr., 1st Lieut., St. Louis, Jefferson Barracks, Mo.
KRUML, Joseph George, 1st Lieut., Ord, Neb., Jefferson Barracks, Mo.
LANNING, Robert Joseph, Captain, Junction City, Kan., Fort Snelling, Minn.
LEONARD, Roosevelt, 1st Lieut., Lyons, Kan., Fort Snelling, Minn.
LIPP, Frank Edward, 1st Lieut., Vinton, Iowa, Fort Des Moines, Iowa.
LONGO, Joseph Alfred, 1st Lieut., Omaha, Fort Des Moines, Iowa.
MACLEOD, Sherburne, 1st Lieut., Wichita, Kan., Fort Snelling, Minn.
MACAULEY, Bernard Joseph, 1st Lieut., Poplar Bluff, Mo., Fort Snelling, Minn.
NASH, Louis Rogers, 1st Lieut., Ingleside, Neb., Fort Snelling, Minn.
ORLIK, Theodore Charles, 1st Lieut., Chamberlain, S. D., Carlisle Barracks, Pa.
SALLADAY, Isaiah Reed, 1st Lieut., Pierre, S. D., Fort Snelling, Minn.

SHANE, Robert Shoemaker, Lieut. Col., Pilot Mound, Iowa, ½ The Governor, Des Moines, Iowa.
SPRONG, Aron Alfred, 1st Lieut., Sterling, Kan., Fort Snelling, Minn.
WESSLING, Alfred Louis, Major, Bethany, Mo., Fort Snelling, Minn.

To Carlisle Barracks

The following additional medical reserve corps officers have been ordered to extended active duty and are to report to Carlisle Barracks, Pa., for a one month refresher course and thence to permanent station, which will be designated by proper authority. This report dates from November 23 through November 29.

AKER, Grover Cecil, 1st Lieut., St. Louis.
BENINCASA, Anthony Vincent, 1st Lieut., St. Louis.
BLANKENSHIP, George William, 1st Lieut., Boonville, Mo.
COUGHLIN, Samuel Thomas, 1st Lieut., Larned, Kan.
DEVEREUX, James Aloysius, Captain, St. Louis.
DREY, Norman Walter, 1st Lieut., St. Louis.
FOWLER, HOLLACE Donald, 1st Lieut., Little Rock, Ark.
GUCCIONE, Joseph, 1st Lieut., St. Louis.
HAGAN, Francis James, 1st Lieut., Wichita, Kan.
HAGEN, Wayne Sigvart, Captain, Minneapolis.
HARMS, Albert Charles, 1st Lieut., Oregon, Mo.
HERMAN, Allen Isadore, 1st Lieut., Springfield, Mo.
HIRST, Otis Grady, Captain, Prescott, Ark.
JOHNSON, John Woodrow, 1st Lieut., Kerkhoven, Minn.
LITTMANN, Lewis Ezekiel, 1st Lieut., St. Louis.
MARX, Paul Donald, 1st Lieut., Lincoln, Neb.
McMILLAN, Orin Perry, 1st Lieut., El Dorado, Ark.
MOSS, Paul, 1st Lieut., Kansas City, Mo.
ODESSKY, Louis, 1st Lieut., St. Paul.
PALMER, Henry Preston, 1st Lieut., Scott City, Kan.
POTEK, David, 1st Lieut., International Falls, Minn.
RITCHIE, Elmer Joseph, 1st Lieut., North Little Rock, Ark.
SCANLAN, Jerome Edward, 1st Lieut., St. Paul.
SCHULTE, Gregory Adrian, 1st Lieut., Joplin, Mo.
WILLIAMS, Mark Frederic, 1st Lieut., Linton, N. D.

Ordered to Fort Snelling

GLEASON, Wallace Anselm, Captain, St. Paul.

NINTH CORPS AREA

The following additional medical reserve corps officers had been ordered to extended active duty by the Commanding General, Ninth Corps Area, up to December 7. The Ninth Corps Area comprises the states of Washington, Montana, Oregon, Nevada, Utah, California and Idaho.

ALNE, Arthur E., 1st Lieut., Fullerton, Calif., Presidio of Monterey and Fort Ord, Calif.
BAER, Irving N., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
BARNARD, James F., 1st Lieut., Arlington, Calif., Presidio of Monterey and Fort Ord, Calif.
BIDWELL, Robert R., 1st Lieut., Santa Monica, Calif., Presidio of Monterey and Fort Ord, Calif.
CLEAVE, David C., 1st Lieut., Belvedere, Marin County, Calif., Presidio of Monterey and Fort Ord, Calif.
COLLINS, Robert F., 1st Lieut., North Hollywood, Calif., Presidio of Monterey and Fort Ord, Calif.
GENDEL, Samuel, 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
GOODWIN, Ralph A., 1st Lieut., Emmett, Ida., 3d Medical Battalion, Fort Lewis, Wash.
HARRISON, Alexander V., 1st Lieut., Los Angeles, Fort MacArthur, Calif. (not Fort Lewis, as stated in THE JOURNAL, December 7).

HEATH, Richard S., 1st Lieut., Inglewood, Calif., Presidio of Monterey and Fort Ord, Calif.
HORNER, Jack C., 1st Lieut., Los Angeles, Presidio of Monterey, Calif.
HUISER, George D., 1st Lieut., Richmond, Calif., Presidio of San Francisco.
KLOSS, Richard G., 1st Lieut., Oakland, Calif., Presidio of Monterey, Calif.
LAMB, Phillip V., 1st Lieut., Angels Camp, Calif., Presidio of Monterey and Fort Ord, Calif.
PASMORE, John L., Captain, Imola, Calif., Presidio of Monterey and Fort Ord, Calif.
POYAS, John L., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
ROSENBERG, Ralph, Captain, San Francisco, Fort MacArthur, Calif.
ROSSI, George J., 1st Lieut., San Francisco, Presidio of San Francisco.
SHEAR, Sidney P., 1st Lieut., Los Angeles, Presidio of Monterey and Fort Ord, Calif.
SHERERTZ, Richard C., 1st Lieut., Modesto, Calif., Presidio of Monterey and Fort Ord, Calif.
TEALL, Ralph C., 1st Lieut., Sacramento, Calif., McClellan Field, Calif.

Relieved

ABRAMOPOULOS, Christos A., Major, reported ordered to extended active duty on report of week ended Nov. 8, 1940, relieved from active duty Nov. 27, 1940.

ORGANIZATION SECTION

OFFICIAL NOTES

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the A. M. A. meeting at Cleveland on June 3, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations, and no revenue is derived from the programs. Therefore, local stations may or may not take the programs, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and broadcast it at another hour or even on another day. It is advisable therefore to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in *THE JOURNAL* and monthly in *Hygia*, *The Health Magazine*.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

December 25.	The Country Doctor.
January 1.*	Otorhinolaryngologist.
January 8.	Your Eyes.

* This program only will be broadcast one hour earlier than the regular scheduled time in order to clear the network for international broadcasts later in the evening.

MEDICAL ECONOMIC ABSTRACTS

MEDICAL CARE FOR MIGRATORY LABOR

The Interdepartmental Committee to Coordinate Social and Welfare Activities has recommended extension of medical care for migratory workers in the report published in the "Social Security Bulletin," September 1940, pages 3 to 15. After describing the work done in California under the Farm Security Administration, the report says:

The committee believes that federal funds should be made available through state and local agencies to assist the states in providing health and medical services for migrants. It recommends, specifically, that the federal funds made available under titles V and VI of the Social Security Act for the fiscal year ending June 30, 1941, be augmented by the sums of \$1 million and \$3 million, respectively, for the purpose of initiating a program to provide essential medical care to needy interstate migrants.

The committee also believes the successful administration of such a program demands that—

1. The state should participate financially in the program.
2. The program should provide both preventive and therapeutic services.
3. Federal funds should be available to all the states in accordance with the need for such grants.
4. The program should be applicable to all occupational groups of interstate migratory laborers.
5. Federal aid should be conditioned on provision for administration by a state agency and on states meeting within three years specified federal requirements covering length of residence within the state.
6. Social investigation, health protection and medical relief for migrants should be provided by the local agencies providing similar services for residents where such agencies exist.

AMOUNT AND TYPES OF MEDICAL CARE

The United States Public Health Service has been giving further analysis to the survey of sickness and medical care first conducted by the Committee on the Costs of Medical Care for 8,758 white families, including a total of 39,185 individuals resident "in 130 localities in 18 states representing all geographic sections."¹ The latest study of these figures is to

determine the amount and type of medical care received by these persons. The total attended cases during the year that these families were kept under observation amounted to 2.9 calls per person. The total calls for those actually attended was 4.6 per case. Eighty-one per cent were attended by private general practitioners, who made 72 per cent of all calls by any type of attendant. These figures are significant in view of the challenge frequently made of the statement that between 80 and 85 per cent of all illnesses can be adequately cared for by a general practitioner. Twelve and five-tenths per cent of all cases were attended by a specialist. Private group clinics attended only 1 per cent of the cases. Three and three-tenths per cent of the illnesses were attended by nonmedical practitioners including osteopaths, chiropractors, Christian scientists and other faith healers, naturopaths, midwives and chiropodists but not dentists.

Patients are classified according to age and sex, and when the diseases characteristic of a single case are excluded the percentage of home calls was about the same for all cases.

As might have been expected, the rate of calls per thousand of population was higher in cities of 100,000 population or more than in smaller cities and rural districts. The same percentage of difference as to population was found for non-medical practitioners.

A somewhat striking difference is found between geographic sections in respect to calls by nonmedical practitioners. Patients in the South gave the least patronage to nonmedical practitioners and California the highest, the ratio being 75 to 451. California patronage of nonmedical practitioners was more than twice as great as that of any other section of the country.

The distribution of doctors' case and call loads according to diagnosis is given in considerable detail and should be of value in calculating the probable cost of any prepayment plan for medical care. In practically all cases the greatest amount of care was required by minor respiratory disease and the second highest usually by accidents. When the cases attended by other practitioners are analyzed quite a different picture is seen. While minor respiratory is still the leading disease treated by osteopaths with rheumatic diseases second, the chiro-

1. Collins, S. D.: Frequency and Volume of Doctors' Calls Among Males and Females in 9,000 Families, Based on Nationwide Periodic Canvasses, 1828-1931, Pub. Health Rep. 55:1977 (Nov. 1) 1940.

practor reverses this order. "Backaches and other ailments" occupy the third place with both, while "nervous" receives much more attention by these types of practitioners than by physicians. When it comes to the number of calls, rheumatic diseases lead in the practice of both osteopaths and chiropractors, making up 13.6 and 14.1 per cent of their entire practice, while they require but 3.2 per cent of the care given by gen-

eral practitioners. The report of the Public Health Service comments on this feature as follows:

The lack of definite diagnoses for illnesses treated only by nonmedical practitioners tends to increase the number of ill defined cases; in spite of this tendency the picture seems reasonably true, namely that it is the various rheumatic and other indefinite chronic pains that bring the patient to a nonmedical practitioner. Aside from this, sprains and other cases where massage therapy is commonly applied also fall into the hands of such practitioners.

WOMAN'S AUXILIARY

Delaware

The annual meeting of the auxiliary to the Delaware Medical Society met in Rehoboth, October 3, with thirty-eight members present.

Weekly meetings for Red Cross work were voted on. A committee was appointed to collect clothes for the British War Relief.

Dr. A. R. Shands, the guest speaker, spoke on the recently opened Nemours foundation, a hospital for crippled children of Delaware.

Iowa

At the executive board meeting of the woman's auxiliary to the Iowa State Medical Society in Des Moines, September 16, Mrs. V. E. Holcombe, national president, addressed the group on the increasing influence and responsibility of women. Also present were Dr. James C. Hill and Dr. John G. de Bey, members of the advisory council. Each addressed the group, giving valuable suggestions regarding the role of the doctor's wife as an individual and the auxiliary as a unit in promoting medical interests.

A recent addition to the state organization was reported as the Upper Des Moines Auxiliary, comprising the counties of Emmet, Dickinson, Clay and Palo Alto.

Nebraska

The auxiliary to the Lancaster County Medical Society met October 7. The speaker was Prof. O. H. Bimson of Lincoln High School, who talked on his experiences as a member of the Educational Policies Commission and the American Youth Commission.

The Omaha-Douglas county medical auxiliary held a Harvest Home Benefit Dinner October 9. Proceeds from the dinner will benefit the projects adopted at the recent membership tea: namely subscriptions to *Hygeia* to all 102 of Omaha's public and parochial schools and contributions to the Community Chest, the School Free Lunch Fund and the Nebraska Tuberculosis Health Camp.

A joint meeting of the tri-county auxiliary No. 1 and the Tri-County Medical Society was held recently at the St. Francis Hospital in Grand Island. The nurses' glee club sang during the dinner hour. At the auxiliary meeting after reports were given by committee chairmen Mrs. Elmer Hansen spoke on auxiliary problems; Mrs. J. G. Woodin, president of the auxiliary, gave a talk on "A Look Ahead," and Mrs. A. D. Broun, state president, addressed the group.

The Woman's Auxiliary to the Adams County Medical Society met at Ingleside. Mrs. L. W. Rork presided. There was a business meeting preceded by a musical program given by the occupational therapy department at Ingleside.

New York

The Woman's Auxiliary to the Albany County Medical Society entertained, September 17, the wives of members of the third district branch to the state medical society, which includes Schoharie, Albany, Rensselaer, Greene, Columbia, Sullivan and Ulster counties. The auxiliaries of Columbia County and of Albany County held their regular meeting at this time and invited doctors' wives of unorganized counties. October 23, the Albany auxiliary was addressed by Dr. Louis Bauer, a member of the medical preparedness committee of the New York State Medical Society.

At the annual dinner of the auxiliary to the Cayuga County Medical Society the sum allotted for the dinner was presented to the American Red Cross. Mrs. G. B. Adams, president-elect

of the woman's auxiliary to the state society, was guest of honor at a tea to which members of the Onondaga County auxiliary were present.

The auxiliary to the Essex County Medical Society was organized, June 4, at the semiannual meeting of the society. Mrs. G. Scott Toune, past state president, Mrs. T. C. Bullard of Saratoga and Mrs. R. F. Johnson of Cayuga gave talks. With the organization of the Essex County auxiliary there are twenty-four counties organized in New York State.

The first meeting of the year in Nassau County was a membership tea, September 24. Guests were greeted by the president of the auxiliary, Mrs. A. C. Martin, and by Dr. Aaron Higgins, president of the county medical society.

The fourth district branch of the state medical society held its annual meeting in Schenectady October 1 and 2. The wives of all the doctors in the district were entertained by the auxiliary. The presidents of counties having auxiliaries acted as hostesses for the day and the wives of the presidents of the unorganized counties and wives of the officers of the district branch were guests of honor.

Ohio

A meeting of the executive board of the Woman's Auxiliary to the Ohio State Medical Association was held in Columbus, October 9, with Mrs. J. Edwin Purdy, the president, presiding. She expressed appreciation that all the members were present and then introduced Mrs. V. E. Holcombe, the national president. Mrs. W. H. Curtiss, Chairman of Organization, reported that about forty counties had organized. The meeting adjourned, to meet in Cleveland in June.

Utah

The auxiliary to the Weber County Medical Society held its first meeting of the year on Monday, October 7, at the home of Mrs. Joseph R. Morrell in Ogden. "Health Insurance" was discussed by Dr. G. M. Fister, and there was music by Mrs. O. S. Daines. Mrs. A. Z. Tanner, Layton, the new president, was in charge.

The Salt Lake County medical auxiliary held a meeting at the Hotel Utah Roof Garden. The first speaker was Dr. E. M. Neher, advisory chairman. The new officers were introduced, and Mrs. John Z. Brown gave some history of the Salt Lake County organization. She introduced those who were present who had served as presidents. Dr. Dee L. Folsom of the Salt Lake Dental Society spoke in the interests of impending legislation of interest to both dentists and doctors in Utah and Salt Lake City.

Wisconsin

The Woman's Auxiliary to the Douglas County Medical Society, with Mrs. E. A. Myers presiding, met October 7 in Superior. Miss Aimee Zillmer of the state health department spoke on "Social Hygiene." For a special project Miss Zillmer was kept in the county for two weeks, being presented to twelve different civic organizations, including all of the P. T. A. groups in the city of Superior, all of the junior and senior high schools in the city and county, the Teacher's College and some special classes in the college.

Red Cross work was started in November by the Manitowoc County auxiliary, of which Mrs. Theodore Tietgen of Manitowoc is president.

The Washington-Ozaukee auxiliary is taking up Red Cross work. At the October 10 meeting two members volunteered to knit and twelve to sew. Mrs. A. H. Heidner of West Bend is the new president.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 2227.

CALIFORNIA

Surgical Meeting.—The Los Angeles Surgical Society held its annual meeting, December 13, with Dr. Rolland Russell Best, associate professor of surgery, University of Nebraska College of Medicine, Omaha, as the guest speaker. His subject was "Indications for the Biliary Flush." Others on the program included:

Dr. George Lawrence Chaffin, Ruptured Diverticulitis of the Colon.
Dr. Emmet A. Pearson, Heterotopic Endometriosis.
Dr. Charles W. Reeder, Long Beach, Idiopathic Segmental Infarction of the Greater Omentum.
Dr. William H. Snyder Jr., Extensive Carbuncle of the Neck.
Dr. Arthur E. Smith, Bilateral Condylar Fracture in a Patient with Multiple Fractures of the Mandible.

Breakfast Club Organized.—Forty-five members of the staff of the Methodist Hospital of Southern California, Los Angeles, have organized a breakfast club which meets at the hospital on the first and third Wednesday morning of the month. Each meeting starts at 7:30 a. m. and ends promptly at 9. Chairmanship of each meeting is chosen by lot. Two cases are presented which have been previously abstracted from actual case reports. Copies are distributed for perusal during breakfast. The names of patient and physician are withheld to stimulate informality and freedom of discussion. A name is drawn from those present and this physician may ask any questions to work up the case. He gives the diagnosis and outlines the treatment that he would follow. This is compared with the chart diagnosis and treatment and general discussion follows. Each of these two cases takes twenty-five minutes, after which a short prepared paper of interest to all is given by one of the members.

ILLINOIS

Conference on Public Health.—The Illinois Conference on Public Health was held in Springfield, December 5-6. Among the speakers were:

Dr. Halbert L. Dunn, Washington, D. C., Using Vital Statistics as a Program Guide.
Howard J. Shughnessy, Ph.D., Chicago, Milk-Borne Disease.
Dr. Robert S. Breakey, Lansing, Mich., Sex Education in High Schools.
Dr. Harry S. Mustard, New York, Public Health in National Defense.
Dr. Richard E. Shope, Princeton, N. J., Epidemiology of Virus Diseases.
Dr. Donald K. Hilbs, Chicago, Chemotherapy in the Treatment and Control of Gonorrhea.

Chicago

Activities of Tumor Institute.—The Chicago Tumor Institute has issued a report of its activities for its first two years. Of 904 patients observed, 613 patients had cancerous lesions, while 301 had benign tumors, inflammatory lesions and other noncancerous conditions. It is of special significance, says the report, that of the 613 cancer patients 262, or 42.7 per cent, had far advanced cancers, and it is sad to reflect that the greater number were cases of accessible forms of cancer easily curable in early stages. Of the total number of patients, 622 were residents of Chicago, 140 came from cities in Illinois outside of Chicago, 130 from twenty-four other states and 12 from six foreign countries. Procedures carried out included 13,269 examinations, 8,846 roentgen diagnoses, 7,756 roentgen treatments, 4,432 radium treatments, 184 minor surgical procedures, seventy-eight surgical procedures, and the making of 278 photographs and lantern slides. An attempt is being made to pursue a five year follow-up of all cancer patients treated at the institute and in the group of 904 observed only 1 patient remained untraced at the end of the first two years. Every patient who was treated has been traced. "Cancerphobia" is attributed to 34 patients of the 904 who came to the institute because of fear they were suffering from cancer. The disease was not found in any of this group. Seventeen, or 50 per cent, are classified as having general phobias, and of the remainder

one third referred their complaints to the breast, one third to the mouth and one third to the gastrointestinal and genito-urinary systems. In the first two years, two courses have been held and instruction has been given to forty-nine qualified radiologists, thirty-six from the United States and thirteen from foreign countries. Eighty physicians from thirty foreign countries visited the institute to study its organization and equipment and consult with the staff on various phases of the cancer problem. The institute was opened in March 1938 and the report covers the period ended March 31, 1940.

INDIANA

Chief of Local Health Administration.—Dr. George M. Brother, Rising Sun, formerly director of district health unit number 4, has been appointed chief of the bureau of local health administration of the state board of health. He succeeds Dr. John W. Ferree, Indianapolis, who recently became director of the board of health. Dr. Brother recently took a degree in public health at Johns Hopkins University School of Hygiene and Public Health, Baltimore. He graduated at Indiana University School of Medicine, Indianapolis, in 1934.

IOWA

Aid for Research.—Grants-in-aid for research have been received recently by the following staff members of the State University of Iowa College of Medicine, Iowa City: Harry M. Hines, Ph.D., of the department of physiology, \$5,000 from the National Foundation for Infantile Paralysis for study of regeneration of nerve and muscle; Dr. William D. Paul of the department of theory and practice, \$3,500 from the Emerson Drug Company for the study of the action of bromides, and Dr. Philip C. Jeans of the department of pediatrics, \$3,000 from the Mead Johnson Company for a continuation of studies on infant nutrition.

KANSAS

Society News.—Dr. Willis H. McKean, Kansas City, addressed the Wyandotte County Medical Society, November 19, on "Surgical Treatment of Empyema" and Dr. Maurice A. Walker, Kansas City, "Minor Surgery in the Office."—Drs. Fred J. McEwen and James B. Fisher addressed the Sedgwick County Medical Society in Wichita, November 19, on "Pulmonary Embolism" and William P. Callahan, "Medical Preparedness." Drs. Rolland Russell Best and Frank Lowell Dunn, both of Omaha, presented the program before the society, November 6; their subjects were, respectively, "Biliary Flush as an Aid in Surgery and Medical Treatment of Biliary Tract Diseases" and "Modern Undernutrition."

LOUISIANA

Changes in Health Officers.—Dr. William C. Summer, Minden, director of the Webster Parish health unit for the past ten years, has resigned to become consultant adviser to the parish health units in eighteen parishes of northern Louisiana. He will be succeeded by Dr. Edmond G. Klamke, New Roads, health director of Pointe Coupee Parish.—Dr. John M. Whitney, Jennings, head of the Jefferson Davis Parish health unit, has been made director of fifteen parish health units in southwestern Louisiana; the area runs from the Texas line to Terrebonne Parish on the south to Pointe Coupee Parish on the north.

Refresher Course.—A refresher course in obstetrics will be conducted at the Louisiana State University Medical Center, January 6-18. The group is limited to eight physicians, so that each may receive individual attention. Additional courses will be offered later in the year. The course is being financed by social security funds allocated to the state by the Children's Bureau, U. S. Department of Labor. Applications of physicians interested in taking the course should be sent to the Maternal and Child Health Division, 313 Civil Courts Building, New Orleans, on or before December 1. Applications will be reviewed by a committee from the state medical society, who will select the physicians to take the course.

NEW JERSEY

District Meeting.—Dr. Frank H. Lahey, Boston, President-Elect of the American Medical Association, addressed a meeting of the Fifth Council District of the Medical Society of New Jersey, December 19, in Woodbury, on "Management of Diseases of the Thyroid." The Gloucester County Medical Society was host.

Special Society Meeting.—Dr. Hyman I. Goldstein, Camden, was elected president of the New Jersey Gastroenterological Society at its annual meeting in Newark, December 2. Dr. Harrison R. Wesson, Montclair, was elected vice president and Dr. Sydney Rosenthal, Newark, secretary. A public meeting will be held by this society February 3, at which a symposium on "Ulcer of the Stomach and Duodenum" will be presented.

NEW YORK

The State Society's Postgraduate Courses.—The council committee on public health and education of the Medical Society of the State of New York has arranged several courses for county societies. A course on general medicine is being presented before the Schoharie County Medical Society on Tuesday afternoons at Cobleskill and the Montgomery County society Tuesday evenings at Amsterdam with the following speakers:

November 19, Dr. David D. Moore, New York, Diabetes Mellitus.
November 26, Dr. Kenneth R. McAlpin, Williamstown, Mass., A General Consideration of Anemia, Both Primary and Secondary.
December 3, Dr. Harold J. Stewart, New York, Digitalis Therapy: Mechanism of Its Action in Congestive Heart Failure.
December 10, Dr. Albert Vander Veer, New York, Asthma.
December 17, Dr. Leslie P. Barker, New York, Syphilis.
January 7, Dr. Homer F. Swift, New York, Rheumatic Fever.
January 14, Dr. John D. Lyttle, New York, Nephritis.

Two courses are in progress for the Nassau County Medical Society. One on pediatrics, arranged in cooperation with the state department of health, has the following schedule:

November 25, Dr. Charles Hendee Smith, New York, Diet of Infants and Children.
December 23, Dr. Hugh Chaplin, New York, Care and Feeding of Prematures.
January 27, Dr. Gaylord W. Graves, New York, Preventive Pediatrics and the Periodic Health Examination.
February 24, Dr. Philip M. Stimson, New York, The Infectious Diseases.
March 24, Dr. Frederick H. Wilke, New York, The Anemias of Childhood.
April 28, Dr. Katharine G. Dodge, New York, Rheumatic Fever, Chorea and Heart Disease.

The following speakers are announced for a course in general medicine in Nassau County:

November 18, Dr. Ralph G. Stillman, New York, The Significance of Laboratory Tests and Methods in the Practice of Medicine.
December 16, Dr. Harry H. Gordon, New York, Endocrine Problems in Adolescence.
January 20, Dr. Norman H. Plummer, New York, Newer Chemotherapeutic Methods.
February 17, Dr. Norman H. Jolliffe, New York, The Relation of Vitamins to Disease.
March 17, Dr. Edward M. Livingston, New York, Abdominal Pain.

New York City

Public Lectures.—The New York Academy of Medicine opened its sixth annual series of "Lectures to the Laity," November 14, with the Linsly R. Williams Memorial Lecture, by Dr. Alan Gregg, on "Humanism and Science." Others in the series are as follows:

Dr. William Healy, Boston, Psychiatry and the Normal Life, December 12.
Dr. Henry E. Sigerist, Baltimore, Paracelsus in the Light of Four Hundred Years, January 23.
Dr. Francis Carter Wood, New York, What We Do Know About Cancer, February 27.
Irwin Edman, Ph.D., New York, Philosophy as Therapy, March 27.
Oscar Riddle, Ph.D., Cold Spring Harbor, The Promise of Endocrinology, April 24.

Dr. Meleney Comes to New York University.—Dr. Henry E. Meleney, associate professor of preventive medicine and public health at Vanderbilt University School of Medicine, Nashville, Tenn., has been appointed Hermann M. Biggs professor of preventive medicine at New York University College of Medicine, effective April 1, 1941. Other appointments announced are:

Dr. Conrad Berens, associate professor of ophthalmology.
Dr. Wendell L. Hughes, clinical professor of ophthalmology.
Dr. Charles W. Lester, assistant clinical professor of surgery.

Dr. Robert F. Pitts, instructor in physiology, has been promoted to assistant professor of physiology.

Dr. Mustard Honored.—The Alumni Association of the De Lamar Institute of Public Health, Columbia University College of Physicians and Surgeons, gave a dinner, November 19, at the Hotel George Washington in honor of Dr. Harry Stoll Mustard, director of the institute. Leonard J. Ciccoli, Ph.D., president of the association, presided, and the speakers were Drs. Mustard; Wilson G. Smilie, professor of public health and preventive medicine, Cornell University Medical College, and Comdr. Charles S. Stephenson, an alumnus, in

charge of the division of preventive medicine, Bureau of Medicine and Surgery, U. S. Navy. Dr. Mustard was appointed last April to succeed Dr. Haven Emerson as director of the institute.

NORTH CAROLINA

Anniversary at Duke University.—The tenth anniversary of Duke University School of Medicine and Duke Hospital, Durham, was observed, November 29-30. An addition to the hospital and a new department of psychiatry were dedicated. Dr. Adolf Meyer, Henry Phipps professor of psychiatry of the Johns Hopkins University School of Medicine, Baltimore, conducted a clinic to mark the opening of the new psychiatric wards, which are named in his honor. The wards provide eighteen beds for the use of the new department. Dr. Richard S. Lyman, formerly of Baltimore, has been appointed professor of psychiatry. The new hospital wing is five stories high and has two hundred rooms providing one hundred and thirteen additional beds and eighty new offices and examining rooms. At the ceremony Dr. Frederic M. Hanes, Florence McAlister professor of medicine, presided. The speakers were Robert L. Flowers, acting president of the university, and Dr. Wilburt C. Davison, dean of the school of medicine. Another feature of the two day program was a clinic at which Dr. Jay M. Arena presided, and addresses were made by Drs. Hanes, David T. Smith, Julian Deryl Hart and Francis Bayard Carter. At a dinner, Friday, at the University Union, the alumni association was formally organized, with Drs. Arena as president; Robert W. Graves, vice president, and J. Lamar Callaway, secretary. All are on the Duke Hospital staff. Duke Hospital received its first patient July 21, 1930, and has since received more than 143,000 patients. The school of medicine opened in October 1930 and has graduated 374 physicians.

OHIO

The Lower Lecture.—Edward A. Doisy, Ph.D., professor of biochemistry, St. Louis University School of Medicine, delivered the third annual Lower Lecture of the Academy of Medicine of Cleveland, November 15. His subject was "Vitamin K and Other Antihemorrhagic Compounds."

Personal.—Dr. Torald H. Sollmann, dean and professor of pharmacology and materia medica, Western Reserve University School of Medicine, Cleveland, received the "degree of merit" of Nu Sigma Nu at the annual convention of the fraternity in Detroit, November 23.—Dr. James C. Elder, Millersburg, has resigned as health officer of Holmes County.

Society News.—Dr. John Scudder, New York, addressed the Academy of Medicine of Cincinnati, November 19, on "Shock: Blood Studies as a Guide to Therapy."—Dr. Edward H. Ryneerson, Rochester, Minn., addressed the Stark County Medical Society, Canton, November 14, on "Diabetes Mellitus and Hyperinsulinism."—A symposium on "Low Back Pain" was presented at a meeting of the Columbus Academy of Medicine, November 18, by Drs. Judson D. Wilson on "Injury to Articular Facets"; Roy J. Secrest, "Herniated Intervertebral Disk," and Harry E. Le Fever, "Hypertrophied Ligamentum Flavum."—Dr. Robert R. Crawford, Mansfield, addressed the Ashland County Medical Society, Ashland, November 15, on the care of fractures.—Dr. Harold Feil, Cleveland, discussed "Cardiac Emergencies and Their Treatment" at a meeting of the Lorain County Medical Society, Elyria, November 12.—Dr. Carlo J. Tripoli, New Orleans, addressed the Montgomery County Medical Society, Dayton, November 15, on "New Developments in the Treatment of Meningitis."

PENNSYLVANIA

Society News.—Dr. Newlin F. Paxson, Philadelphia, addressed the Delaware County Medical Society, Chester, November 14, on "Chronic Nephritis and Pregnancy."—Dr. George P. Müller, Philadelphia, addressed the Cambria County Medical Society, Johnstown, November 14, on "Cancer of the Stomach."—The Lycoming County Medical Society held an all day meeting in Williamsport, November 8, with the following speakers: Drs. Leonard G. Rowntree, Philadelphia, on cardiovascular disease; Lewis C. Scheffey, Philadelphia, on gynecology; Harrison F. Flippin, Philadelphia, and Dale C. Stahl, Harrisburg, a symposium on pneumonia.—The annual William Moore Guilford Memorial Clinic was presented by the Lebanon County Medical Society, Lebanon, November 26. Dr. Baldwin H. E. W. Lucke, Philadelphia, conducted the clinic on "Edema of Renal Origin."—Dr. Marshall M. Lieber, Philadelphia, addressed the Washington County Medical Society, Washington, November 6, on "Newer Concepts on the Mechanism of Inflammation and Shock—Some Practical Considerations."

GENERAL

Outbreaks of Influenza.—An extensive outbreak of an apparently mild type of influenza was reported December 16 in Alexandria, La. This city has recently nearly doubled its normal population of 30,000 owing to the influx of army camp workers and others who have flocked there in view of the military training program at Camp Beauregard nearby. Several thousand cases of influenza are said to have developed chiefly among the camp construction workers and others, many of whom were living under unsatisfactory housing conditions. No cases were reported among the soldiers at Camp Beauregard. The *Chicago Tribune* reports that the influenza epidemic in the Western states, now waning in California, has spread to Washington and Oregon. Schools were closed in Bellingham, Wash., December 13 and in Portland December 16. Influenza has also been reported in Texas and Kentucky.

Grants for Research in Endocrinology.—Requests to the National Research Council Committee for Research in Endocrinology for aid during the fiscal period from July 1, 1941 to June 30, 1942 will be received until Jan. 31, 1941. Application blanks may be obtained by addressing the Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington, D. C. In addition to a statement of the problem and research plan or program, the committee wants information on the proposed method of attack, the institutional support of the investigation and the uses to be made of the sum requested. No part of any grant may be used by the recipient institution for administrative expenses. Applications for aid of endocrine research on problems of sex in the narrower sense cannot be given favorable consideration, but the committee will consider support of studies on the effects of sex hormones on nonsexual functions, for example on metabolism.

Fund Available for Research.—The next meeting of the American Academy of Arts and Sciences to consider applications for assistance in scientific research will be held February 15. Income from the Permanent Science Fund, according to agreement and declaration of trust, shall be applied by the academy to such scientific research as shall be selected "... in such sciences as mathematics, physics, chemistry, astronomy, geology and geography, zoology, botany, anthropology, psychology, sociology and economics, history and philology, engineering, medicine and surgery, agriculture, manufacturing and commerce, education and any other science of any nature or description, whether or not now known or now recognized as scientific, and may be applied to or through public or private associations, societies, or institutions, whether incorporated or not, or through one or more individuals." Additional information may be obtained from the chairman of the Committee on the Permanent Science Fund, Prof. John W. M. Bunker, Massachusetts Institute of Technology, Cambridge, Mass.

Psychiatric Association Plans Public Education Program.—The committee on public education of the American Psychiatric Association announces the appointment of twelve regional chairmen to cooperate with the press and otherwise "to foster the dissemination of sound psychiatric information to the public." The chairmen are Drs. Franklin G. Ebaugh, Denver; Ralph C. Hamill, Chicago; Titus H. Harris, Galveston, Texas; Richard H. Hutchings, Utica, N. Y.; George S. Johnson, San Francisco; William C. Menninger, Topeka, Kan.; Merrill Moore, Boston; Arthur P. Noyes, Norristown, Pa.; Winfred Overholser, Washington, D. C.; Thomas A. Ratliff, Cincinnati; Newdigate M. Owensby, Atlanta, Ga.; and Karl M. Bowman, New York. In addition to providing the press of these regions with an authoritative source of information on psychiatric matters, the association will stress its policy with regard to mental hospital standards, it was said. "One of the principal aims of this organization will be to acquaint the public with the fact that a well staffed, well equipped hospital for the care of the mentally ill is not a luxury, but a basic necessity in any civilized community," the statement said.

Annual Forum on Allergy.—Allergists of the Middle West will hold their third annual forum to review progress in the clinical study of allergy in Indianapolis, January 11-12, at the Claypool Hotel. Methods of instruction will include study groups under different instructors, exhibits, special lectures, question and answer periods and symposiums. The annual Forum Lecture will be delivered Sunday by Dr. Bela Schick, New York, on "Allergy, Hypersensitiveness and Immunity." Dr.

Schick will receive a gold medal honoring him for "distinguished and outstanding contributions in the field of allergy." The other special lectures will be delivered by Dr. Albert D. Ruedemann, Cleveland, on "Allergic Manifestations in the Eye," and by Dr. Malcolm M. Cook, St. Louis, "Water and Electrolyte Metabolism in Allergy." The symposiums will be on "Bronchial Asthma," with Dr. Ben Z. Rappaport, Chicago, as moderator; "Insects as Allergens," Dr. Harry L. Huber, Chicago, and "Allergic Headache," Dr. Theodore L. Squier, Milwaukee. All physicians in good standing in their local medical societies will be welcome. There will be a registration fee of \$5. Registrations should be mailed to Dr. Tell Nelson, 636 Church Street, Evanston, Ill.

Special Society Elections.—Dr. John H. Moore, Grand Forks, N. D., was chosen president-elect of the Central Association of Obstetricians and Gynecologists at its recent annual session in Indianapolis and Dr. Thomas B. Sellers, New Orleans, was installed as president. Other officers include Drs. Minnie L. Maffett, Dallas, vice president, and William F. Mengert, Iowa City, secretary-treasurer. New Orleans was selected as the place of the 1941 meeting, the exact date to be announced later.—Dr. Bruce H. Douglas, Detroit, was elected president of the Mississippi Valley Conference on Tuberculosis at the annual meeting in St. Paul, October 2-4. Donald E. Pratt, executive secretary of the Missouri Tuberculosis Association, was elected vice president, and A. W. Jones, executive secretary of the St. Louis Tuberculosis and Health Society, was reelected secretary. Dr. George C. Turner, Chicago, was elected president of the Mississippi Valley Sanatorium Association, which met in conjunction with the tuberculosis conference. Dr. Francis F. Callahan, Pokegama, Minn., was elected vice president and Dr. Henry S. K. Willis, Northville, Mich., secretary.—Dr. Marcus Pinson Neal, Columbia, Mo., was chosen president-elect of the Southern Medical Association at the annual meeting in Louisville, Ky., November 12-15. Dr. Paul H. Ringer, Asheville, N. C., was elected president, taking the place of Dr. Quitman U. Newell, St. Louis, the president-elect, who died a few days before the meeting. Drs. Ernest Lee Heflin, Louisville, and James R. Bloss, Huntington, W. Va., were elected vice presidents. Next year's meeting will be in St. Louis.—Ernest Carroll Faust, Ph.D., New Orleans, was chosen president-elect of the American Society of Tropical Medicine at its annual meeting in Louisville, Ky., November 12-15, in conjunction with the Southern Medical Association. Dr. Thomas T. Mackie, New York, was installed as president; Dr. Fred L. Soper, Rio de Janeiro, Brazil, was made vice president, and Dr. E. Harold Hinman, Wilson Dam, Ala., secretary.—Dr. Earl E. Kleinschmidt, Chicago, was chosen president-elect of the American School Health Association at its recent annual meeting and Dr. Amos L. Beagler, Denver, was inducted into the presidency. Dr. Helen Irene Ahrens Cary, Portland, Ore., and Lon W. Morrey, D.D.S., Chicago, were chosen vice presidents. Dr. Arville O. DeWeese, Kent, Ohio, is the executive secretary-treasurer.—Gobind Behari Lal, New York, science editor of International News Service and the Hearst newspapers, was elected president of the National Association of Science Writers at its annual meeting. Robert D. Potter, science editor of the *American Weekly*, New York, is vice president; Miss Jane Stafford, medical writer, Science Service, Washington, D. C., secretary, and Stephen J. McDonough, science writer, Associated Press, Washington, treasurer.

Government Services

The Government Needs Technicians

The U. S. Civil Service Commission requests applications for positions as senior medical technician at \$2,000 a year, medical technician at \$1,800, and assistant medical technician at \$1,620. The senior technician may offer general subjects or specialize in roentgenology; the medical technician and the assistant may have their choice of surgery, roentgenology or general subjects. This announcement is an amendment of an earlier one which did not include "general" in the optional subjects. Applications must be on file with the commission at Washington, D. C., not later than December 30 if from states other than the following: Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. For the Western states the deadline is January 2.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 13, 1940.

The Chemotherapy of War Wounds

At the Medical Society of London a discussion took place on chemotherapy in war wounds. Col. Max Page said that it was not until 1939 that surgeons took any interest in the use of sulfonamide derivatives in the treatment of wound infection. Experimental work, mainly on mice, indicated that they had a prophylactic value. Plans were made for trying them in the war, but the nature of the campaign in France and Flanders allowed only sporadic attempts as far as recorded evidence went. His own impression was that the incidence of secondary infection in wounds treated with sulfanilamide was lower than might have been expected from the last war. The condition in which prophylactic use of a sulfonamide was probably good was a late wound, twenty-four or thirty-eight hours or perhaps a week after infection, requiring operation and suggesting the possibility of a flare-up. If a full dose was given by mouth beforehand, intervention would be safer. In treatment a few doses would on most occasions deal with an acute streptococcal infection but not with a chronic infection. When the infection was in the blood the drug was not of the same value as when it was in the body tissues. The same held for gas gangrene.

Colonel Colebrooke said that definite results were to be expected from careful use of sulfonamide derivatives. The first was the prevention of hemolytic streptococcus infection. But the great majority of the wounded in war were not infected with hemolytic streptococci at the time of the injury. Their infection occurred at any time within a week afterward as a hospital infection. A sulfonamide derivative would be valuable in a case of secondary operation in which there was a suspicion of hemolytic streptococcus infection. Prophylactic treatment should be administered in four hourly doses. It might also be possible to arrest infection by prompt and vigorous action. In long-standing or superficial cases, such as old burns and road accidents which had led to infection, the application of sulfanilamide powder gave astonishingly good results.

Mr. W. H. Ogilvie said that infection seemed to be a far less serious problem in this war than in the last. The explanation was not simple. The wounded were far less fatigued and dehydrated; their clothes were cleaner; many of the weapons were less damaging to the tissues than the shell and hand grenades which were so much used in the last war. He thought that the streptococci and anaerobic organisms of today were feeble compared with their ancestors of 1914-1918. But after making these allowances much credit must go to chemotherapy. In the wounded from the evacuation of Dunkirk chemoprophylaxis when started early put the patients in good condition, while those who arrived infected at the hospital in whom chemotherapy was started immediately after débridement soon showed repair and clean granulation. The contrast between the wounds of those who had been given a sulfonamide derivative in transit and those who had not was great. The latter when admitted two or three days after being wounded were most heavily infected. On being put on a sulfonamide derivative they had a temperature which rarely rose above 100 F. or remained elevated more than three or four days. Sir Thomas Dunhill referred to 65 patients treated in the hospital, all extremely ill. Their knees and elbows were shattered and ankles broken. Pus was soaking through the plaster, and the stench was beyond belief. In the last war he would have felt that three fourths would require amputation and that streptococcal septicemia would occur. They were treated by fixation and a sulfonamide derivative for a number of days until it was felt that appropriate doses had been

given. Two died from secondary hemorrhage and one from gas gangrene, but all the rest did well. He believed that three fourths of the results was due to fixation and the rest to the sulfonamide derivative. Together they seemed to be able to scotch the spread of infection.

Gas Gangrene

The War Wounds Committee of the Medical Research Council and the Committee of London Sector Pathologists have published a review of gas gangrene based on the experience of the last great war and on recent experience in Spain, France and elsewhere. As these committees are composed of leading surgeons and pathologists the pamphlet, which is published by the government, is authoritative. For prophylaxis, excision of contaminated war wounds at the earliest opportunity is recommended. But when injured men come under observation only at a later period, when organisms have already reached the living tissues bordering on the wound cavity or when the wound is passing through a stage of physiologic reaction to injury, the time for prophylactic excision has passed and the surgeon should aim at providing adequate drainage by incision. In late cases, however, in which there is any suspicion of gangrenous infection of muscle, the wound must be opened up and the muscles implicated must be ruthlessly excised.

Recent laboratory experiments indicate that the best available treatment, in addition to surgery, for the established disease is a combination of antitoxin and chemotherapy with sulfapyridine or sulfanilamide. The serum and the drug seem to have a synergic action, the former neutralizing the bacterial toxin, while the latter exercises a bacteriostatic effect on the organism. The antitoxin should be administered, preferably intravenously, at the earliest possible moment. The dose of polyvalent antitoxin recommended is 7,500 international units of *Clostridium welchii*, 3,750 of *Clostridium septicum* and 2,500 of *Clostridium oedematiens*, repeated as necessary. The first dose of sulfapyridine or sulfanilamide should be 2 Gm. dissolved in hot citric acid or lemon solution. Subsequent doses, starting two hours later and continued four hourly for two days, should be 1 Gm. uncrushed. After the first two days the dose should be gradually reduced as the condition improves, but the interval between the doses should not be more than six hours for several days. Small doses, e. g. 3 Gm. daily, should be continued for three or four days after the temperature has become normal. The duration of treatment and the total dosage will vary somewhat, but the latter should seldom exceed 35 Gm.

In cases in which the surgeon has to operate on a wound in which anaerobic infection is already established, preoperative sulfapyridine or sulfanilamide by mouth and antitoxin intravenously may be useful in preventing the spread of infection. The first dose of the drug should be 3 Gm., which should, if possible, be given two hours before operation so as to secure a high concentration in the blood when the wound is disturbed.

Marriages

DAVID BRAINARD GREGG, Greensboro, N. C., to Miss Mary Page Newton of Charleston, S. C., October 17.

WILLIAM C. BEHEN, Lansing, Mich., to Miss Rose Lucille Megerle of Newport, Ky., October 14.

DUWARD O. WRIGHT, Fort Payne, Ala., to Miss Harriet D. Harton at Conway, Ark., October 5.

JOHN J. SCHOFF, Media, Pa., to Miss Charlotte Fullerton of Swarthmore, November 8.

DAVID ROSENBLUM to Miss Esther Shamir, both of Los Angeles, September 21.

JOHN JIBB THORNTON to Miss Marion Faye Gager, both of Cleveland, October 11.

Deaths

Edgar Alphonso Hines * Seneca, S. C.; Medical College of the State of South Carolina, Charleston, 1891; member of the House of Delegates of the American Medical Association from 1910 to 1928 and from 1930 to 1940; vice chairman of the state board of health for many years and one of the founders of the board's bureau of child hygiene; past president of the South Carolina Pediatric Society and the Piedmont Postgraduate Clinical Assembly; member of the American Academy of Pediatrics; fellow of the American College of Physicians; in 1913, session chairman of the International Congress of School Hygiene in Buffalo; for many years trustee and chairman of the school board; on the staff of the Oconee County Hospital; superintendent of the Anderson County Hospital, Anderson, for 1915; secretary of the South Carolina Medical Association; secretary-treasurer of the Oconee County Medical Society; editor in chief of the *Journal of the South Carolina Medical Association*; chairman of the Committee on Medical Preparedness for South Carolina; aged 73; died, November 27, of coronary occlusion.

Philip King Brown * San Francisco; Harvard Medical School, Boston, 1893; assistant in nervous diseases, University of California Medical School in 1894, associate professor of clinical medicine from 1896 to 1898 and instructor of animal pathology from 1896 to 1899; associate in medicine and instructor of clinical pathology, Cooper Medical College from 1899 to 1902; member of the Association of American Physicians and the American Clinical and Climatological Association; served in various capacities and at various times on the staffs of the Southern Pacific Hospital, Stanford University Hospital and the City and County Hospital, San Francisco; secretary of the board of directors, founder and for many years medical director of the Arequipa Sanatorium, Manor; aged 71; died, October 29, of coronary thrombosis.

Lemuel Payson Adams * Oakland, Calif.; University of Vermont College of Medicine, Burlington, 1899; member of the House of Delegates of the American Medical Association in 1925; senior fellow of the Pacific Coast Surgical Association; a founder of the American Association for the Surgery of Trauma and of the American Board of Surgery; fellow of the American College of Surgeons; chief of the East surgical staff of the Alameda County Hospital, Oakland, and the Fairmount Hospital, San Leandro; a director and member of the staff of Peralta Hospital, Oakland; aged 65; died, October 27, of coronary embolism.

Jackson Thornwell Witherspoon * New York; Johns Hopkins University School of Medicine, Baltimore, 1928; member of the Indiana State Medical Association; formerly instructor and later assistant professor of gynecology at Tulane University of Louisiana School of Medicine, New Orleans, and assistant professor and subsequently associate professor of gynecology at the Indiana University School of Medicine, Indianapolis; author of "Clinical Pathological Gynecology"; at one time editor of *Modern Medicine*; aged 40; died, October 19, at his home in Darien, Conn.

John Henry Rishmiller * Gibbon, Minn.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1891; an Affiliate Fellow of the American Medical Association; fellow of the American College of Surgeons; past president of the American Association of Railway Surgeons; formerly chief surgeon of the Soo Line; at one time on the staff of the City Hospital and Swedish Hospital, Minneapolis; aged 74; died, October 15, of cerebral embolism, cerebral hemorrhage and essential hypertension.

George Robert Cruickshank, Windsor, Ont., Canada; Victoria University Medical Department, Coburg, 1886; L.R.C.P., Edinburgh, Scotland, 1890; past president of the College of Physicians and Surgeons of Ontario; member of the Senate of the University of Toronto for many years; medical officer of health for Windsor from 1914 to 1919, and helped to organize the present board of health; in 1919 was president of the Ontario Health Officers Association; aged 80; died, October 8.

Roland Beatty Tupper * Fresno, Calif.; Cooper Medical College, San Francisco, 1910; at one time assistant clinical professor of medicine at his alma mater; member of the American College of Chest Physicians; served during the World War; formerly on the staff of St. Luke's Hospital, San Francisco; aged 54; on the staffs of the Fresno General Hospital and the Burnett Sanitarium, where he died, October 30, of coronary occlusion.

Henry Edward Menage, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1892; member of the Louisiana State Medical Society and the American Academy of Dermatology and Syphilology; professor of dermatology emeritus at his alma mater; veteran of the Spanish-American War; formerly on the staff of the Charity Hospital; aged 68; died, October 22, of arteriosclerotic heart disease.

Samuel Jackson Pate, Woodville, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1905; member of the State Medical Association of Texas; past president of the Jefferson County Medical Society; served during the World War; on the staffs of the Hotel Dieu Hospital and St. Therese Hospital, Beaumont; aged 62; died, October 17, of chronic nephritis, myocarditis and hypertension.

Frederick Francis Andrews * Revere, Mass.; Harvard Medical School, Boston, 1905; for many years school physician; formerly member of the board of health; on the staffs of the Winthrop (Mass.) Community Hospital, Whidden Memorial Hospital, Everett, and the Chelsea (Mass.) Memorial Hospital; aged 68; died, November 5.

William A. Spurgeon, Muncie, Ind.; Physio-Medical College of Indiana, Indianapolis, 1875; member of the Indiana State Medical Association; past president of the Indiana State Board of Medical Registration and Examination and of the American Confederation of Reciprocating Medical Licensing Boards; aged 88; died, October 21.

Monroe T. Smith, Warren, Pa.; Medico-Chirurgical College of Philadelphia, 1889; member of the Medical Society of the State of Pennsylvania; past president of the Warren County Medical Society; for many years on the staff of the Warren General Hospital; aged 74; died, October 25, of coronary embolism.

Francis William Briggs * Havre, Mont.; State University of Iowa College of Medicine, Iowa City, 1905; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Sacred Heart and Deaconess hospitals; aged 66; died, October 27, in Great Falls, of heart disease.

Henry R. Krasnow, Chicago; Chicago College of Medicine and Surgery, 1914; instructor of dermatology at the University of Illinois College of Medicine; aged 57; on the staffs of the Research and Educational Hospital and the American Hospital, where he died, October 31, of coronary thrombosis.

Raymond Braxton Kicklighter, Glennville, Ga.; University of Georgia Medical Department, Augusta, 1928; member of the Medical Association of Georgia; served during the World War; aged 46; died, October 29, in the Veterans Administration Facility, Oteen, N. C., of tuberculosis.

Florence Gertrude Mikulski, Buffalo; University of Buffalo School of Medicine, 1924; member of the Medical Society of the State of New York and the American Society of Anesthetists; on the staffs of the Millard Fillmore and Lafayette General hospitals; aged 46; died, October 24.

Earle Haggett MacMichael, Englewood, Fla.; Harvard Medical School, Boston, 1910; served during the World War; member of the New England Society of Psychiatry; aged 56; died, October 27, in Venice of hypertensive heart disease, arteriosclerosis and arthritis deformans.

George J. Hess, Wayne, Neb.; Detroit College of Medicine, 1894; member of the Nebraska State Medical Association; also a pharmacist; president of the Wayne County Medical Society; aged 72; died, October 25, in a hospital at Norfolk of cerebral hemorrhage.

Clinton C. Tyrrell, Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1906; member of the Minnesota State Medical Association; served during the World War; aged 63; died, October 22, of chronic myocarditis and arteriosclerosis.

John Gilmer Reynolds, Chatham, Va.; Hospital College of Medicine, Louisville, Ky., 1904; member of the Medical Society of Virginia; aged 71; died, October 25, in the Memorial Hospital, Danville, of arteriosclerosis, myocarditis and bronchopneumonia.

Eb Nichols Gray, Houston, Texas; Jefferson Medical College of Philadelphia, 1883; member of the State Medical Association of Texas; on the staffs of the Memorial, Hermann and Jefferson Davis hospitals and St. Joseph's Infirmary; aged 79; died, October 19.

Charles Sumner Reed, Agency, Iowa; Drake University Medical Department, Des Moines, 1902; member of the Iowa

State Medical Society; past president of the Wapello County Medical Society; aged 70; died, October 4, of cerebral hemorrhage.

Preston Winford Pearson, Emory, Texas; Memphis (Tenn.) Hospital Medical College, 1903; member of the State Medical Association of Texas; past president of the Hunt-Rockwell-Rains Counties Medical Society; aged 57; died, October 12.

Wilbur Moate Scott * Milledgeville, Ga.; University of Maryland School of Medicine, Baltimore, 1912; served during the World War; member of the Southeastern Surgical Congress; owner of the Scott Hospital; aged 49; was found dead, October 31.

William Bedwell Harrell Sr., Thomaston, Ala.; Louisville (Ky.) Medical College, 1905; member of the Medical Association of the State of Alabama; aged 59; died in October at a hospital in Birmingham of a severed artery, self inflicted.

William Alonzo Smith, Panther Burn, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; member of the Mississippi State Medical Association; aged 57; died, October 6, in the King's Daughters' Hospital, Greenville, of pneumonia.

James Harvey Hudson, Merrill, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1883; formerly member of the school board, mayor and postmaster; aged 81; died, October 24, of multiple sclerosis.

Edwin Cornue Hoff * Detroit; Cleveland Homeopathic Medical College, 1901; fellow of the American College of Surgeons; aged 65; on the staff of the Grace Hospital where he died, October 23, of heart disease and prostatectomy.

Walter Wesley Sawyer, Elizabeth City, N. C.; University of Maryland School of Medicine, Baltimore, 1903; member of the Medical Society of the State of North Carolina; aged 60; died, October 20, of coronary thrombosis.

Nathan I. Kithcart, Columbia City, Ind.; Medical College of Ohio, Cincinnati, 1881; member of the Indiana State Medical Association; formerly secretary of the Whitley County Medical Society; aged 89; died, October 29, of myocarditis.

Albert Earl Sumner, Richmond Hill, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1894; consulting physician to the Roosevelt Hospital, New York; aged 73; died, October 31.

Owen F. Moran, Milledgeville, Ga.; Atlanta Medical College, 1888; member of the Medical Association of Georgia; formerly county commissioner of health; aged 73; died, October 31, of myocarditis and arteriosclerosis.

Francis Joseph Noonan, Troy, N. Y.; Albany Medical College, 1905; served during the World War; on the staff of the Troy Hospital; aged 59; died, October 18, of cerebral hemorrhage, arteriosclerosis and diabetes mellitus.

Bert Luther Kennedy, Dalton, Ga.; Birmingham (Ala.) Medical College, 1911; member of the Medical Association of Georgia; aged 59; died, October 17, in the Newell Sanitarium, Chattanooga, Tenn., of coronary occlusion.

John H. Heidelman, Ronan, Mont.; Cincinnati College of Medicine and Surgery, 1891; formerly a member of the Indian Service; aged 74; died, September 29, at the St. Patrick Hospital, Missoula, of coronary occlusion.

Melvin D. Hereford * Staten Island, N. Y.; University of Kansas School of Medicine, Kansas City, Kan., 1922; served during the World War; on the staff of the Richmond Memorial Hospital; aged 43; died, October 25.

Henry Learen Applewhite, Archer City, Texas; Southern Methodist University Medical Department, Dallas, 1914; member of the State Medical Association of Texas; aged 53; died, September 6, in a hospital at Olney.

James P. Womack, Nashville, Tenn.; University of Tennessee Medical Department, Nashville, 1886; assistant to the chair in physiology at his alma mater, 1890-1891; aged 79; died, October 28, of cerebral hemorrhage.

Francis Joseph Harrington, Fall River, Mass.; Maryland College of Eclectic Medicine and Surgery, Baltimore, 1914; aged 47; was found dead, October 14, of heart disease and chronic dilatation of the esophagus.

William Armine Humphrey, Columbus, Ohio; Hahnemann Medical College and Hospital, Chicago, 1883; fellow of the American College of Surgeons; aged 80; died, October 30, of arteriosclerotic heart disease.

Horace Hampton Hilliard, Canton, Texas; Baylor University College of Medicine, Dallas, 1917; member of the State Medical Association of Texas; served during the World War; aged 50; died, October 14.

Harry Willard Waterous, Galva, Ill.; Rush Medical College, Chicago, 1885; member of the Illinois State Medical Society; aged 81; died, October 24, in East Pepperell, Mass., of coronary occlusion.

Bernard Weiss * South Ozone Park, N. Y.; Long Island College Hospital, Brooklyn, 1929; on the staff of the Queens General Hospital, Jamaica; aged 36; died, October 20, of coronary thrombosis.

Arthur Wallace Winch, Sanford, Maine; Baltimore Medical College, 1906; served during the World War; aged 61; died, October 13, in the Deaconess Hospital, Boston, of pulmonary tuberculosis.

Victor Hugo Miller, Lakeland, Fla.; University of Louisville (Ky.) Medical Department, 1912; served during the World War; aged 53; died, October 16, in the Morrell Hospital of coronary thrombosis.

William Orville Wilkes, Waco, Texas; University Medical College of Kansas City, Mo., 1885; member of the State Medical Association of Texas; aged 77; died, October 17, of coronary sclerosis.

Roscoe Wesley Swan, Worcester, Mass.; Harvard Medical School, Boston, 1882; member of the Massachusetts Medical Society; aged 80; died, October 13, in the Holden (Mass.) District Hospital.

George Jackson Hill, Boston; Harvard Medical School, Boston, 1903; member of the Massachusetts Medical Society; formerly on the staff of the Children's Hospital; aged 61; died, October 29.

John Paul Hiebert * Minneapolis; Northwestern University Medical School, Chicago, 1905; on the staffs of the Eitel, Abbott and Asbury hospitals; aged 63; died, October 11, of carcinoma of the pancreas.

John T. Iles, Ewing, Texas; University of Arkansas School of Medicine, Little Rock, 1911; aged 63; died, October 16, in the Angelina County Hospital, Lufkin, of cardiovascular renal disease.

Joseph O. King, Ridge, Md.; Baltimore University School of Medicine, 1895; member of the Medical and Chirurgical Faculty of Maryland; aged 67; died, October 31, of pulmonary tuberculosis.

Charlotte Margaretha Sekler Koester, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; aged 69; died, October 2, of pancreatitis.

Kary Gibbon Parker * Mansfield, Ohio; Miami Medical College, Cincinnati, 1903; for many years on the staff of the Ohio State Reformatory; aged 65; died, October 24, of pneumonia.

John Roscoe Varney, Old Town, Maine; Baltimore Medical College, 1896; member of the Maine Medical Association; aged 77; died, October 25, of arteriosclerosis and pulmonary infarction.

Lloyd Thomas Reed, Gravity, Iowa; St. Louis College of Physicians and Surgeons, 1900; member of the Iowa State Medical Society; aged 62; died, October 17, of coronary occlusion.

Isaac H. Treece, Findlay, Ohio; Eclectic Medical Institute, Cincinnati, 1887; aged 77; died, October 24, in the Findlay Hospital of a wound received when his gun accidentally exploded.

Abraham Lincoln Trevaskis, Turtle Creek, Pa.; Starling Medical College, Columbus, 1892; member of the Medical Society of the State of Pennsylvania; aged 80; died, October 28.

Henry H. Clark, Minneapolis; College of Physicians and Surgeons of Chicago, 1893; member of the Minnesota State Medical Association; aged 76; died, October 31, of carcinoma-tosis.

Charles Joel Sage * New York; University of Vermont College of Medicine, Burlington, 1931; aged 36; died, October 18, in the Mount Sinai Hospital of acute myelogenous leukemia.

Jonas Ruby, Chicago; Chicago College of Medicine and Surgery, 1917; for many years school health officer; aged 54; died, October 21, in the American Hospital of coronary occlusion.

James D. Stuart, Washington, D. C.; Columbia University Medical Department, Washington, 1892; member of the Medical Society of the District of Columbia; aged 75; died, October 18.

Moses James Ferguson, Mexico, D. F., Mexico; University of Nashville (Tenn.) Medical Department, 1905; aged 58; died in October of injuries received in an automobile accident.

George A. Noon, Listie, Pa.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1890; member of the Medical Society of the State of Pennsylvania; aged 81; died, October 12.

Albert Sidney Stemler, Washington C. H., Ohio; Eclectic Medical Institute, Cincinnati, 1898; member of the Ohio State Medical Association; aged 66; died in October in Cleveland.

Willie Gregor Spires, Gaskin, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1916; formerly member of the county school board; aged 55; died, October 19.

Jesse Braxton Higgins, Indianapolis; Fort Wayne (Ind.) College of Medicine, 1901; aged 62; died, October 27, in the Veterans Administration Facility of coronary disease.

Frank Horan Gunn, Eau Claire, Wis.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1895; aged 68; died, October 13, of arteriosclerotic heart disease.

Napoleon J. Caron, South Hero, Vt.; Laval University Faculty of Medicine, Quebec, Canada, 1899; aged 69; died, October 23, of carcinoma of the lungs with metastasis.

John Walter Hertridge Jr., St. Louis; Meharry Medical College of Walden University, Nashville, Tenn., 1938; aged 28; died, October 6, of pulmonary tuberculosis.

Lloyd Howe Mott, Los Angeles (licensed in Oregon in 1912); on the staff of the Veterans Administration Facility, West Los Angeles; aged 53; died in October.

George E. French Ⓢ Elyria, Ohio; Western Reserve University Medical Department, Cleveland, 1888; for many years city health officer; aged 76; died, October 30.

William M. Van Der Volgen, Seattle; Kentucky School of Medicine, Louisville, 1877; Medical College of Ohio, Cincinnati, 1887; aged 84; died in October.

Reginald Myron Wildish Ⓢ Webster City, Iowa; University of Nebraska College of Medicine, Omaha, 1911; aged 55; died, September 30, of cardiac embolism.

William James Pillsbury, Baltimore; University of Maryland School of Medicine, Baltimore, 1889; aged 72; died, October 29, of cerebral hemorrhage.

Henry Andrew Life Ⓢ Harlingen, Texas; Barnes Medical College, St. Louis, 1899; aged 66; died, October 21, in the Masonic Hospital, Cherokee, Okla.

Lawrence Henry Oliver, Waupun, Wis.; Marquette University School of Medicine, Milwaukee, 1916; aged 54; died, October 30, of coronary occlusion.

George Tapscott Snead, Pungo, Va.; Medical College of Virginia, Richmond, 1880; formerly member of the state legislature; aged 83; died, October 30.

Walter A. Jenkins, Church Point, La.; Louisville (Ky.) Medical College, 1887; aged 80; died, October 15, of diabetes mellitus, nephritis and myocarditis.

Spencer De Witt Guy Ⓢ Lansing, Mich.; Rush Medical College, Chicago, 1917; served during the World War; aged 47; died, October 26, of pellagra.

Edwin B. Boots Ⓢ Terre Haute, Ind.; Indiana University School of Medicine, Indianapolis, 1930; aged 40; died, October 7, of a gunshot wound.

George Henry Belding, Milwaukee; Milwaukee Medical College, 1903; formerly a dentist; aged 77; died, September 15, of chronic endocarditis.

Alexander Neil MacLeod, Winnipeg, Man., Canada; Manitoba Medical College, Winnipeg, 1893; aged 72; died, October 11, of cerebral hemorrhage.

William McKee Thome, Salem, Ore.; Jefferson Medical College of Philadelphia, 1897; aged 71; died, October 22, of carcinoma of the prostate.

Isabella Holdom, Minneapolis; Michigan College of Medicine and Surgery, Detroit, 1897; aged 81; died, October 23, of cardiac decompensation.

John Earle Jenner, Vancouver, B. C., Canada; Trinity Medical College, Toronto, 1883; L.R.C.P., London, 1883; aged 83; died, October 28.

William Herbert Marshall, Weiser, Idaho; Trinity Medical College, Toronto, Ont., Canada, 1899; aged 66; died, October 18, in Boise.

Thomas Benjamin Smith, Bracey, Va.; Jefferson Medical College of Philadelphia, 1881; aged 81; died, October 15, of cerebral hemorrhage.

George L. Shoemaker, Jennings, La.; Chicago Homeopathic Medical College, 1891; aged 80; died, October 21, of coronary thrombosis.

William Henry Loechner, Omaha; Omaha Medical College, 1901; aged 63; died, October 28, of carcinoma of the head of the pancreas.

Charles Huston Minor, New York; Ohio State University College of Homeopathic Medicine, Columbus, 1920; aged 46; died, September 25.

Samuel S. Guerrant, Callaway, Va.; Medical Department of Tulane University of Louisiana, New Orleans, 1891; aged 73; died, October 28.

Morgan Biddle Jennings, Streator, Ill.; Rush Medical College, Chicago, 1886; aged 77; died, November 16, in St. Mary's Hospital.

James Thompson Longest, Pontotoc, Miss.; University of Tennessee Medical Department, Nashville, 1903; aged 68; died, October 24.

Howard Cousins Fairbanks Ⓢ Tonawanda, N. Y.; University of Buffalo School of Medicine, 1909; aged 54; died, October 13.

Alvin Dennett Holmes, Hudson, Mass.; Medical School of Maine, Portland, 1883; aged 84; died, October 24, of chronic myocarditis.

Walter Jay Insley, Columbus, Ohio; Bennett College of Eclectic Medicine and Surgery, Chicago, 1887; aged 83; died, October 26.

Walter Bryant Guy, St. Augustine, Fla.; Boston University School of Medicine, 1899; aged 70; died, October 3, of coronary thrombosis.

William James Brown, Boston; Tufts College Medical School, Boston, 1906; aged 60; died, September 15, in Plymouth.

Walter A. Gatlin, Paris, Texas; Memphis (Tenn.) Hospital Medical College, 1902; aged 67; died, October 25, of coronary occlusion.

Richard W. Carter, Chicago; Fort Wayne (Ind.) College of Medicine, 1893; aged 70; died, October 25, of chronic myocarditis.

Archibald M. McKennon, Clarksville, Ark.; Jefferson Medical College of Philadelphia, 1874; aged 88; died, October 23.

Francis Edward Carroll, Boston; Harvard Medical School, Boston, 1890; aged 78; died, September 10, in Saugus.

William Douglas Swan, Hamilton, Ont.; University of Toronto Faculty of Medicine, 1921; aged 50; died, October 23.

Alexander Douglas Taylor, Daytona Beach, Fla.; Rush Medical College, Chicago, 1875; aged 86; died, October 5.

Andrew J. Hays, Weslaco, Texas; Keokuk (Iowa) Medical College, 1891; aged 79; died, October 15, of myocarditis.

William Tecumseh Pittman, Spickard, Mo.; Rush Medical College, Chicago, 1892; aged 70; died, October 31.

Joseph A. Roth, Chicago; Harvey Medical College, Chicago, 1905; aged 66; died, October 14, of diabetes mellitus.

Eugene Clair Wasson, Cambridge Springs, Pa.; Baltimore Medical College, 1905; aged 62; died, October 19.

Thomas Z. Clower, Moreland, Ga.; Southern Medical College, Atlanta, 1893; aged 70; died, October 5.

George William May Ⓢ Manchester, Conn.; Milwaukee Medical College, 1895; aged 80; died, October 23.

James Griffin Elrod, Dutton, Ala.; Chattanooga (Tenn.) Medical College, 1902; aged 82; died, October 29.

Victoria Sarah Ernst, Bridgewater, N. S., Canada; Halifax Medical College, 1900; aged 84; died, October 4.

Joseph Ira Esch, La Farge, Wis.; Eclectic Medical Institute, Cincinnati, 1898; aged 71; died in October.

CORRECTION

Dr. Pearson Is Not Dead.—The obituary notice of Dr. Charles Birdsall Pearson of Anaheim, Calif., which appeared in *THE JOURNAL*, November 30, page 1905, was erroneous. Our source of information was a clipping from the *Grand Blanc, Mich., Press*, dated Oct. 10, 1940.

Correspondence

THE EFFECT OF ALCOHOL ON DRIVING SKILL

To the Editor:—The recent article "The Effect of Alcohol on Driving Skill" (*THE JOURNAL*, November 9, p. 1600) brings out a number of interesting facts but may lead to erroneous conclusions if not carefully scrutinized. An ingenious test of driving skill, including both steering and braking, showed that the two skills were more closely correlated than either or both with the exact concentration of alcohol in the blood stream. However, it should be noted that the subjects showed a remarkably similar concentration of alcohol in the blood after the test dose, in no instance varying by more than 0.03 per cent from the average concentration to be expected (chart 1) and almost all lying in the zone characterized by the committees of the American Medical Association and the National Safety Council, as well as most students of the subject, as of "suggestive" or "presumptive" rather than of "conclusive" or "prima facie" significance. Even in this narrow zone, the coefficient of correlation of 0.485, more than six times its probable error, is impressive. If the data had extended over the higher ranges, in which the chemical test is conclusive, as well as over the lower ranges, in which it distinguishes so usefully between the "had been drinking" and the "under the influence" group, a much higher degree of correlation would have undoubtedly appeared. As a matter of fact, the only four persons shown in chart 2 with sufficient alcoholic concentration in the blood to have been convicted by the chemical test alone all showed more than 15 per cent loss of efficiency in driving ability by the tests here reported.

The tests used appear to have been well calculated to bring out differences in driving skill, resulting from changes in reaction time and neuromuscular coordination. As emphasized in the preliminary report of the committee of the American Medical Association on this subject, the early effects of alcohol which may lead to automobile accidents are rather in the sphere of judgment, discretion and disposition than of the more mechanical skills here tested. The slightly intoxicated expert chauffeur may be much better able than the sober occasional driver to pass tests in steering and braking abilities but may also be more apt to take chances or be careless when not consciously being tested. The subject's fallacious impression that skill is improved during the influence of alcohol, noted here as in previous studies, also leads to greater dangers.

The contention that the chemical tests for intoxication penalize the drinking rather than the drunken driver is just the reverse of the facts. It is just the finding that a driver who has been drinking but has less than 0.05 per cent of alcohol in the blood generally fails to show other evidences of intoxication, while the one with more than 0.15 per cent may be shown to be under the influence if sufficiently examined, which makes this test of differential value, as compared with merely smelling the breath or showing the bottle.

It is still conceivable that a person might be found who can have a concentration of alcohol in the blood stream above 0.15 per cent and still fail to show any evidence of the effect of the alcohol on the tissues. Despite thousands of tests, however, and public appeals for the discovery of such person, no such instance has yet been verified. The search should be continued, as further study of such a case might be of great value for our understanding of the nature of tolerance to alcohol. Its occurrence, however, is still unproved.

If one disregards their comments and conclusions, the work of Newman and Fletcher may be accepted as a valuable contribution toward the evaluation of the status of the "borderline case" of the driver with a concentration of alcohol between 0.05

and 0.15 per cent. Practically every worker in this field, as well as the committees of the American Medical Association and the National Safety Council, have urged the use of other evidence in addition to, and in support of, the value of the chemical test, and the performance of the latter in duplicate, or with different samples, in questionable cases. The possibility of technical errors in the performance of the tests, as well as still unknown possibilities in their interpretation, should not be overlooked. The article on false positive serologic tests for syphilis in *THE JOURNAL* just following the paper by Newman and Fletcher, however, indicates how a similar valuable test in another field in medicine may be safeguarded rather than ignored. Further studies of tolerance to alcohol and the factors involved in automobile accidents are still greatly to be desired. At present, however, it may be emphatically reiterated that the determination of the alcoholic concentration of the breath or body fluids remains the most reliable single factor in arriving at a correct conclusion as to the degree of intoxication.

EMIL BOGEN, M.D., Olive View, Calif.

To the Editor:—The recent paper on "The Effect of Alcohol on Driving Skill" by Newman and Fletcher (*THE JOURNAL*, November 9, p. 1600) presents conclusions which are at variance with the majority of scientific investigations on the effects of alcohol. Their report demonstrates the extreme confusion which may result from varying conceptions of the terms "drunk" and "intoxicated." Some writers have maintained that any demonstrable deviation from normal behavior produced by alcohol constitutes alcoholic intoxication. By such a rigid definition most persons may be considered intoxicated following exceedingly small amounts of alcohol such as are contained in a single cocktail or "highball." The opposite extreme is indicated by the criterion often employed by bartenders in determining whether or not a customer may legally be sold further quantities of liquor. This view is perhaps best illustrated by the old barroom quatrain:

He is *not* drunk who from the floor
Can rise again and drink once more.
But he is drunk who prostrate lies
And can neither drink nor rise.

There is a world of difference between these two extremes in defining the term "drunk." When Newman and Fletcher state "Public sentiment is definitely against the drunken driver but not against the drinking driver," all can agree with them in principle. The really important question which must be answered is When does a drinking driver become a drunken driver? Certainly it is long before he reaches the staggering stage of alcoholic intoxication. As was suggested in *THE JOURNAL* ("The Subintoxicated Driver," May 2, 1936, p. 1580) four years ago, serious impairment of driving ability occurs before the ordinary indications of "intoxication" are observable; hence the use of the term "subintoxicated driver." The public associates the term "drunk" with a stage of alcoholic intoxication characterized by staggering gait and confused or slurred speech. Apparently on such a basis Jetter (cited by Newman and Fletcher in support of their thesis) made his clinical diagnosis of acute alcoholic intoxication. Such standards, while entirely suitable for purposes of hospital classification, are hardly adequate for diagnosis of the influence of alcohol on motorists.

The use of the term "under the influence of alcohol" seems to avoid the many deep-seated connotations which, through long usage, adhere to such words as "drunk" or "intoxicated." This condition might be defined as that state at which the effect of alcohol renders a person unfit to perform the particular task which he is attempting. To evaluate fairly the influence of alcohol requires one to take into consideration not only the effects of the alcohol which is circulating through

the body of that person but also the type of activity in which he is engaged. Thus a man may have taken several "high-balls" and seated himself in his home to listen to a radio program. For such a purpose he might be considered to be entirely sober. But if this same man were to undertake a task involving quick and accurate response to stimuli and the use of sound judgment, such as driving a high powered automobile through crowded city streets, he would be fairly classified as "under the influence of alcohol." The loose use of the terms "drunk" and "intoxicated" gives rise to much unnecessary confusion.

The psychologic tests of driving skill reported by Newman and Fletcher illustrate the difficulty in setting up an experimental routine which will measure the desired variable to the exclusion of all others. With reference to tests on the influence of alcohol, these difficulties have been admirably stated by Jellinek and McFarland (*Analysis of Psychological Experiments on the Effects of Alcohol, Quart. J. Studies on Alcohol* 1:272 [Sept.] 1940). Apparently what Newman and Fletcher have measured was impairment of driving skill due to the effect of alcohol plus improvement due to practice. Little wonder, therefore, that they find such poor correlation between alcohol concentration in the blood and their "loss of driving skill." The most eloquent practical demonstration of the correlation between alcohol content of body fluids and driving skill is to be found in the Evanston survey (Holcomb, R. L.: *Alcohol in Relation to Traffic Accidents, THE JOURNAL*, Sept. 17, 1938, p. 1076). A statistical study of the data was made to determine a motorist's chances of finding himself in an Evanston hospital following an automobile accident. Depending on the concentration of alcohol in the blood stream, these probabilities were as follows:

Alcohol in Blood, per Cent	Chances of Hospitalization Following an Automobile Accident
0	1
Less than 0.07.....	3
0.07 to 0.11.....	5
0.11 to 0.15.....	15
Over 0.15	55

It is not reasonable to expect perfect correlation between the dose of any drug and the effect which it produces (Nelson, E. E.: *Variability in Response to Drugs, THE JOURNAL*, Oct. 7, 1939, p. 1373). However, within the limits of normal biologic variation which my experience has indicated to be about 10 to 15 per cent in the case of alcohol (McNally, W. D.: *Toxicology, Chicago, Industrial Medicine*, 1937, p. 659), all persons, regardless of previous experience in the use of alcohol, are equally under the influence of alcohol when they have the same concentration of alcohol in their circulating blood. That determinations of alcohol in the blood leave much to be desired cannot be denied. However, they do serve as an excellent adjunct in the correct interpretation of less quantitative clinical indications of the influence of alcohol. Until better practical and more reliable methods can be found, one may safely continue to employ the methods recommended by the American Medical Association Committee to Study Motor Vehicle Accidents (*THE JOURNAL*, May 27, 1939, p. 2165) and embodied in the National Safety Council's program for safe driving practice.

The use of our highways is not an inherent individual right such as the rights of free speech, free assembly and freedom of worship. It is a privilege conferred by the communities in which we live and may be legally abridged in any way which seems in the interest of public safety and welfare. Society must be free to take effective steps in controlling the ever mounting toll of deaths and injuries due to highway accidents.

C. W. MUEHLBERGER, PH.D., Chicago.

Coroner's Toxicologist, Cook County
Coroner's Laboratory.

To the Editor:—In the article by Newman and Fletcher, "The Effect of Alcohol on Driving Skill" (*THE JOURNAL*, Nov. 9, 1940, p. 1600), are certain discrepancies which might not be perceived.

The authors give experimental data which apparently justify their attack on the "injustice" of the figure of 0.15 per cent alcohol in the blood, which has been set by committees of both the American Medical Association and the National Safety Council as the point at which 100 per cent of persons "tolerant" or otherwise suffer a definite impairment in their driving ability, to the extent that it comes within the meaning of most state laws concerning drunken driving.

They state that the purpose of their experimental work was to investigate the correlation between impairment of driving ability and the 0.15 per cent concentration of alcohol in the blood. Their data of ninety-eight trials on 65 subjects are presented in the form of a pinpoint chart percentage of impairment over normal performance against concentrations of alcohol in the blood. They say that it shows a poor correlation between the two. It does just that and nothing more. The validity of the recommended figure of 0.15 per cent remains unaffected, for the following reasons:

1. Eighty results were between approximately 0.06 and 0.12 per cent, nine between 0.12 and 0.14 per cent, one close to 0.15 per cent and three above 0.15 per cent. The majority of their results were therefore obtained at concentrations much below 0.15 per cent. The four at or above 0.15 per cent prove nothing.

2. The fifteen minute trial periods preceding the actual tests were totally inadequate to eliminate any progressive improvement from this factor. A fifteen minute trial could not possibly have resulted in a plateau of performance for each subject.

3. It is a well known fact that many persons with alcohol concentrations of the blood below 0.15 per cent have a degree of unaffected will power which they can summon to their aid, if there is a reason for them to do so, to compensate to a considerable degree for the effect of the alcohol. This factor in itself may reasonably be held accountable for the poor correlation that the authors found. It is difficult to avoid this compensatory effect in any study which involves performance observation at low concentrations of alcohol. The subject cannot help but be aware that he is expected to make as good a showing as he can. At these low concentrations the occasional unquestionable better performance in such tests is in my opinion due entirely to a compensatory effort over and above that needed to counteract the alcohol. The subject gives a better performance not because of any bettering effect of the alcohol but in spite of it.

It is my sincere belief, based on nearly four years of observing and running blood and urine alcohol tests on actual drunken drivers to a total of between 300 and 400 that, if by some unattainable means every drunken driver's physical condition could be observed unknown to him, no disagreements between concentrations and effects would ever be observed. One sees practically perfect agreements at higher concentrations, because in practically all persons this mechanism then either no longer functions or it is not powerful enough to overcome all the effects of the alcohol.

Whether this occasional exhibition of compensatory mechanism, fairly frequent at low concentrations but becoming rare at higher ones, is due to a progressive loss in will power (apace with progressive impairment in other functions), to a variability in the development of individual will power or to a complex interplay of the two is difficult to say. The important point to keep in mind is that intoxicated persons do not make any effort to exert this compensatory mechanism while driving a car. It never occurs until the person is arrested and is under observa-

tion for his condition. One must remember that, in the ultimate analysis, blood and urine tests are made to determine the stage of intoxication of the subject while he was driving a car and not necessarily after various extraneous factors which unavoidably follow his arrest have entered the picture. These factors are well known to be able to modify the relation between the concentration of alcohol in the blood and the observable effect.

No one has yet succeeded in devising an apparatus to be used in the laboratory in testing driving ability which will take into account all factors, including judgment and estimation of risks, which play a part in determining what an intoxicated person will do, or fails to do, when behind the wheel of a car.

Up to now in only one known instance in the United States has such a study been made wherein the subjects actually drove a car. This was reported in the *Pennsylvania Medical Journal* for December 1932 by Drs. H. A. Heise, Benjamin Halporn and Alfred G. Dietze. The results were considerably different than those of Dr. Newman and Mr. Fletcher. In Dresden, Germany (*THE JOURNAL*, May 7, 1938, p. 1617), a series of tests were made on a large number of volunteers. At a concentration of 100 mg. of alcohol per hundred cubic centimeters of blood, there were 87 per cent of the drivers incapacitated and at 140 mg. 100 per cent.

Newman and Fletcher should repeat their experiment and see to it that the following points are observed: 1. Their subjects should be given doses of alcohol large enough to insure their blood alcohol being at or slightly above 0.15 per cent. 2. Care should be taken that the factor of compensation is eliminated as much as possible by using other than medical students and physicians as subjects and avoiding any hint to the subject, intentional or otherwise, that he is expected to try to drive better because of the alcohol. No suggestion (such as that of a signaling green light) should be given the subject that his alinement of radiator cap with the truck is faulty other than that given by his own judgment. 3. A longer practice period should be given and a plateau definitely established before the alcohol is administered. If this is done, my opinion is that Dr. Newman will obtain a considerably different result.

D. F. DAVIS,

City Health Department, Lincoln, Neb.

To the Editor:—The article "The Effect of Alcohol on Driving Skill" by Newman and Fletcher (*THE JOURNAL*, November 9, p. 1600), questions the value of chemical tests for intoxication. This paper demands an answer, since the conclusions of the authors are warranted neither from their own experimental data nor from their interpretation of the writings of others.

The authors direct their attack particularly to the recommendations of the Committee on Tests for Intoxication of the National Safety Council, and incidentally to the 1939 Report of the Committee of the American Medical Association for the Study of Problems of Motor Vehicle Accidents. These committees have agreed that certain levels of alcohol in the blood or their equivalents in other body fluids are associated with a definite loss of that clearness of intellect and self control which an individual would normally possess. Although the committees realize that there is no minimal figure that can be set at which there will be no effect from alcohol, they agree that all persons are definitely inferior to their normal capabilities when the alcohol concentration exceeds 0.15 per cent. (To reach a blood alcohol concentration of 0.15 per cent, the average sized adult must fail to oxidize from 3 to 4 ounces [90 to 120 cc.] of absolute alcohol.)

The reason for the disagreement is obviously the failure of Newman and Fletcher to realize that there is a vast difference

between the poorly defined terms of *drunkenness* and *intoxication*, and the well defined "under the influence of alcohol."

The National Safety Council Committee recommends that trial courts adopt the definition of the phrase "under the influence of alcohol" as laid down by the Supreme Court of Arizona:

"The expression 'under the influence of intoxicating liquor' covers not only all the well known and easily recognized conditions and degrees of intoxication but any abnormal mental or physical condition which is the result of indulging in any degree in intoxicating liquors, and which tends to deprive him of that clearness of intellect and control of himself which he would otherwise possess. If the ability of the driver of an automobile has been lessened in the slightest degree by the use of intoxicating liquors, then the driver is deemed to be under the influence of intoxicating liquor. The mere fact that the driver has taken a drink does not place him under the ban of the statute unless such drink has some influence upon him lessening in some degree his ability to handle said automobile."—*Steffani v. State*, 42 Pac. (2nd) 615.

The fact that a skilled driver under the influence of alcohol may be able to drive better than an ordinary sober person does not in any way clash with the definition.

The published results of the authors' experiments, involving the use of a machine which measures steering ability and reaction time, do not refute the conclusions of the committees of the American Medical Association and National Safety Council. On the contrary, the four persons whose blood alcohol concentrations exceeded 0.15 per cent all showed 16 per cent or more loss of efficiency, which would definitely place them "under the influence."

The authors state that performance of their test of simple steering is a better criterion of intoxication than is blood alcohol. My experiments along similar lines (*Medicolegal Aspects of Drunkenness*, *Pennsylvania M. J.* 36:190 [Dec.] 1932) but under actual driving conditions indicated that the ability to perform the routine of driving was not always obviously impaired in persons who were under the influence of alcohol according to chemical tests. However, the performances of acts which were not routine, such as backing the car and manipulations demanding judgment, were poorly performed. A simple incident is responsible for abandonment of this type of test: a truck swerved across the path of the test car, narrowly avoiding a collision. When I said to the driver, who at that time tested about 0.13 per cent, "Say, wasn't that a narrow escape from that truck?" he looked at me with an expressionless face, saying, "What truck?" After this incident, less dangerous experiments involving skill, judgment and intelligence were instituted. By these tests it was a simple matter to demonstrate definite impairment in judgment and personality long before coordination was affected. In all my experiments, involving more than 200 persons, no one was found who was able to reach a blood alcohol concentration of 0.10 per cent without showing definite changes for the worse.

The conclusions of the authors are not warranted from their interpretation of the writing of Bogen (*Drunkenness: A Quantitative Study of Acute Alcoholic Intoxication*, *THE JOURNAL*, Oct. 29, 1927, p. 1508), himself a member of the Committee on Tests for Intoxication of the National Safety Council. Bogen reports the cases of persons who were adjudged intoxicated or drunk and not persons who were proved to be "under the influence."

Jetter's subjects (*Studies in Alcohol*, *Am. J. M. Sc.* 196:475, 487 [Oct.] 1938) were adjudged intoxicated by a criterion which he himself set. In a recent article (*The Chemical and Clinical Diagnosis of Acute Alcoholism*, *New England J. Med.* 221:1019 [Dec. 28] 1939) he makes his position clear:

While only 50 per cent of cases in a group of habitual drinkers will be clinically intoxicated at a blood alcohol level of 0.15 Gm. per 100 cc., sufficient impairment of faculties will be present in even this type of individual to make him a menace as a driver.

Finally, I heartily disagree with the authors' implication that persons of greater skill than the average should not be penalized for their only offense of having alcohol in their blood stream. They would condone the resulting loss of driving

skill as long as the drivers managed to stay above "minimum standards of skill." They forget that the average driving skill results in a slaughter of more than 30,000 people in this country each year and that the superior driver has no legal or moral right to lower his efficiency toward the average.

HERMAN A. HEISE, M.D., Milwaukee.

Chairman, Committee of the American Medical Association to Study Problems of Motor Vehicle Accidents.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SERUM FOR POLIOMYELITIS

To the Editor:—What is the present status of convalescent serum in the treatment of anterior poliomyelitis?

J. G. Woodin, M.D., Grand Island, Neb.

ANSWER.—A simple and unchallenged answer cannot be given on the beneficial effect of convalescent serum in the treatment of acute anterior poliomyelitis. The reasons lie somewhat in the variability of the disease itself and, as in other acute infectious diseases, in the fact that the disease is self limiting. Although the early workers in this field were unanimous in stating that convalescent serum tended to prevent the spread of paralysis and aided in the recovery of paralysis, present day workers view this early opinion with skepticism. At present the matter is to be considered somewhat undecided but with the potential field of usefulness of serum markedly narrowed.

Reaction against the wholesale indiscriminate use of convalescent serum dates from the report of Park on the New York epidemic of 1931 (Therapeutic Use of Antipoliomyelitis Serum in Preparalytic Cases of Poliomyelitis, *THE JOURNAL*, Sept. 24, 1932, p. 1051; *New York State J. Med.* 33:91 [Jan. 15] 1933). This author reported on the serum treatment of half of the patients from a group of 927 in the preparalytic stage. The amount of paralysis judged by muscle examinations made shortly after the administration of serum and six months later showed no difference between the group that received serum and that which had received none. The data from this report were questioned by many workers in the field because alternate cases were not treated and serum was given to those seen late in the natural course of the preparalytic disease. It has since been shown that patients in the preparalytic stage, seen two or more days after the onset of paralysis, are already selected naturally and are destined to have little paralysis. The situation is further complicated by the fact that a large share of all cases diagnosable in the "preparalytic state" are actually nonparalytic cases; 71.5 per cent of 531 patients according to one published review (Harmon, P. H.: Poliomyelitis: Experimental and Theoretical Basis for Serum Therapy, *Am. J. Dis. Child.* 47:1179 [June] 1934). Harmon also failed to find statistical evidence for the beneficial use of convalescent serum. The incidence of paralysis and the apparent prevention of paralysis by serum were the same according to these statistics regardless of whether the serum used was convalescent serum, the antistreptococcus horse serum of Rosenow or "normal" human serum, which contains antiviral antibodies active in the test tube. Likewise, Kramer, Aycock, Solomon and Thenebe (Convalescent Serum Therapy in Preparalytic Poliomyelitis, *New England J. Med.* 206:432 [March 3] 1932) in the 1931 epidemic in Connecticut failed to find any difference in a control group of patients who did not receive convalescent serum and a similar group of patients who had received this agent.

The majority of workers have preferred to continue their observations. Convalescent serum admittedly does no harm and it has not yet been proved that it is valueless. Some favorable results have been recorded in recent years. Cowie, Parsons and Lowenberg have reported no residual paralysis in 80 preparalytic cases treated with both human convalescent serum and transfusions from "normal" adults. They also reported symptomatic improvement in certain paralytic cases. However, that serum was responsible solely for this turn of events must be viewed with skepticism in view of the well known tendency of

the disease to halt spontaneously and suddenly in the face of apparent advancing paralysis (Clinicopathologic Observations on Infantile Paralysis: Report of 125 Acute Cases with Special Reference to the Therapeutic Use of Convalescent and Adult Blood Transfusions, *Ann. Int. Med.* 8:521 [Nov.] 1934).

The most continuous experience with the use in convalescent serum in the treatment of this disease has been that of pediatricians and public health workers in the state of Illinois. The last official report originating from this source was that of Levinson (Poliomyelitis in the Chicago Area, *Illinois M. J.* 70:296 [Sept.] 1936). This author reported on the treatment of 149 preparalytic cases occurring in Chicago between 1931 and 1935. In the 1936 epidemic a mortality rate of 39 per cent was reported in bulbar cases (the mortality in untreated cases was 90 per cent). Only 8 patients from 53 preparalytic cases became paralyzed after serum was administered. The mortality in the latter group was zero and only 2 had slight residual paralysis. While the incidence of paralysis in this group of preparalytic cases was not dissimilar to those not receiving serum, it should be pointed out that the incidence of residual paralysis was practically zero. A recent report emanating from California (Geiger, J. C.; Burlingame, R. W., and Miller, R. C.: Convalescent Serum in Acute Anterior Poliomyelitis: Report of a Study of 168 Patients, 69 Treated, 98 Untreated, *California & West. Med.* 51:303 [Nov.] 1939) states that "the cases with entrance paralysis show little or no variation between treated and untreated in percentage in partial or complete recovery or death. Among those considered early cases, but with entrance weakness, the percentages of partial or complete recovery showed equally small or no variation in the treated and untreated. The early cases with no weakness or paralysis, however, indicate that a different viewpoint can be stressed. The preparalytic cases (27), when treated with convalescent serum, recovered without any residual paralysis. Therefore, in this series of cases of this type, or in early cases of acute anterior poliomyelitis with clinical and laboratory evidence substantiating the diagnosis, it would appear that convalescent serum is of benefit."

All the experimental evidence deduced from the use of convalescent human and monkey antiserum in the disease in monkeys clearly shows that the experimental disease is not benefited by serum. Such evidence should not be considered in evaluating the results in man, as the simian disease is entirely different in its onset, course and outcome. The disease in man is notoriously more variable and more mild both in extent of paralysis and in mortality.

The aggregate of opinion in recent years, as evidenced by the opinions and quotations given, would favor the use of human convalescent serum or transfusions from at least two or three normal adult blood donors during the preparalytic stage, while in cases of early paralysis in which the paralysis has ceased to advance and the temperature has dropped to normal serum should not be used. There are those who continue to use serum in early paralytic poliomyelitis, but no evidence can be said to favor such a procedure. From the practical point of view, it must be pointed out that the differentiation between preparalytic poliomyelitis and the early paralytic stages of this disease is exceedingly difficult.

LOCAL TREATMENT OF NASOPHARYNX IN "INFLUENZA"

To the Editor:—For the past two years I have noted a vesicular pharyngitis quite regularly in patients having the classic symptoms of influenza. This observation has been described as frequently accompanying the nasal pharyngitis that results from influenza. Is there any local treatment other than ephedrine shrinkage of the nasal pharynx and local application of silver salts that might be more specific as a remedy for the cough and gastrointestinal irritation that accompanies this lesion?

Henry E. Davidson, M.D., Lead, S. D.

ANSWER.—The use of weak ephedrine solutions in the nose by means of drops, use of an atomizer or following the recommendations of Proetz, is a useful method of treating the rhinitis and rhinopharyngitis following the so-called "flu." The vesicles, after they have ruptured, may be treated by the application of silver salts together with hot nonirritating gargles. To the extent that the reduction of nasal secretion prevents the cough which is due to purulent matter dropping into the larynx and trachea, the cough will be improved. That part of the cough which is due to a laryngotracheitis should be dealt with by the use of mixtures containing codeine, by steam inhalations, bed rest and the like.

The gastrointestinal irritation is probably not due to the local nose and throat condition but is a part of the general picture and has to be dealt with in a common sense manner. This calls for a proper bland diet, the avoidance of drastic cathartics and similar rational measures.

MEDICAL EXAMINATIONS OF FOOD HANDLERS

To the Editor:—Please advise me whether an examination of feces is desirable on food handlers in an institution where 1,700 young women eat in three large dining halls and where the following public health measures are carried out: complete examination of all food handlers, laborers and maids, including routine roentgen examinations of the chest, urinalysis and blood agglutination tests for typhoid, proteus, tularemia, abortus and the paratyphoid groups. We have never made any examination of stool specimens and accordingly I am asking your advice as to the advisability of this practice. We are anxious to take every precaution to insure the health of our people. I might add that the dishes are boiled under high pressure in all eating places, including all tea rooms about the campus, and that all food handlers have special instructions about cleansing hands, finger nails and their bodies in general.

William B. Brown, M.D., Columbia, Mo.

ANSWER.—In general, routine examination of food handlers in large numbers is an expensive procedure. A single stool examination gives little information. It is not unusual to have a number of negative stool cultures followed by a positive culture in the case of a typhoid carrier. In an institution where every possible protection is desired and, especially, if the turnover in employees is not great, routine examination of stools is of some value. The limitations of the possibilities of detecting cases or carriers from a single examination must be remembered, however. If there is a history of typhoid it is desirable that repeated stool cultures be made.

From the point of view of protection of those served by the employees, little could be expected of the agglutination tests for typhoid, proteus (typhus fever, Rocky Mountain spotted fever), tularemia, undulant fever and paratyphoid. With the exception of typhoid and paratyphoid fever, direct transmission from patient to patient either does not occur in these diseases or is an insignificant factor in their spread.

The agglutination test is of little value in the detection of typhoid carriers. Probably the education of food handlers is the most important disease prevention factor. Food handlers should have knowledge of the practical facts concerning the transmission of communicable diseases and should have medical attention available for the investigation of any signs of illness.

AMENORRHEA

To the Editor:—A white woman aged 26, married, weighing 106 pounds (48 Kg.) complains of small and poorly developed breasts. She says that they were well developed seven years ago. The menses began at 13, were regular every twenty-eight days and lasted five or six days. There was no dysmenorrhea. She had a miscarriage at three and one-half months eight years ago, an appendectomy seven years ago, a miscarriage at four and one-half months six years ago and a cholecystectomy three years ago. She has had amenorrhea since the last miscarriage six years ago. In 1937 she received two roentgen treatments over the pituitary followed by two regular menstrual periods. Physical examination revealed no abnormalities of the heart, the pulse is 80 and blood pressure 110 systolic, 65 diastolic. The abdomen shows the scar over the gallbladder area and midline below the umbilicus. The uterus is small but palpable. What procedure can be followed?

M.D., New Jersey.

ANSWER.—Unless the young woman is desirous of having children there is no reason to try to induce uterine bleeding. However, if there is a psychic disturbance because of the absence of menstruation, bleeding may be induced by so-called withdrawal therapy. A simple way to accomplish this is to administer 10,000 international units of estrone hypodermically three times a week for two weeks. Usually bleeding occurs about eight or ten days after the last injection. However, this form of therapy will produce only one bleeding episode. If the physician desires to produce cyclic bleeding he will have to repeat the series of injections every month.

If the patient is anxious to have a baby it is essential to find out whether the ovaries are functioning. Two things must be done. One is to obtain an endometrial biopsy at weekly intervals to see the type of endometrium which is present. If successive biopsies show a change from proliferative to secretory endometrium, this is evidence of the presence of ovulation. It is possible to have ovulation without menstruation and vice versa. If biopsies reveal secretory endometrium there is no need to give the patient treatment for the amenorrhea. Since she ovulates she can conceive.

If, on the other hand, the biopsies show persistent proliferative endometrium or hyperplasia the patient does not ovulate. In addition to endometrial biopsies a study of the urine should be made to determine the amount of gonadotropic hormone. If there is an excessive amount of this hormone it indicates that the ovaries are not functioning properly. An attempt may be made to stimulate ovulation by the administration of the gonadotropic substance obtained from pregnant mares' serum but the results have not been encouraging.

The amenorrhea may be overcome by radiation therapy of the pituitary gland. However, this treatment should be carried out only by a skilful roentgenologist.

The patient should have a basal metabolism study. If the rate is low, thyroid medication should be given, because not infrequently thyroid extract overcomes amenorrhea in women with hypothyroidism.

UNUSUAL PAIN AT CLOSE OF MENSTRUAL PERIOD

To the Editor:—A woman aged 21 with no physical defects and a perfectly normal menstrual history has severe pains starting at the end of each menstrual period. These pains are of the same type as tic douloureux; that is, a severe pain comes on lasting two minutes with complete relief for six or eight minutes, only to be repeated. They increase in severity until she is given a hypodermic of morphine one fourth grain (0.016 Gm.). The pain is to the right of the median line, apparently over the right ovary. There is absolutely no tenderness on deep pressure. Ordinary analgesics have no effect. The condition has been going on for years. No pelvic examination has been made. Can you give me any enlightenment on this case?

L. C. Howe, M.D., Muscatine, Iowa.

ANSWER.—This is a puzzling type of pain for which there does not seem to be any physiologic reason. Therefore it is difficult to recommend any therapy. Endocrine treatment will almost certainly be of no avail. If the patient is a virgin, a bimanual recto-abdominal examination should be made to rule out a possible pelvic lesion. Otherwise a vaginal examination should be made. If no abnormality is found, a pelvic sympathectomy may be justified because of the long duration of the pain and because of the strong likelihood of making the patient a morphine addict.

LATE FALL ASTHMA

To the Editor:—A woman, aged 26, living in midwestern Wisconsin, complains of asthma-like attacks of many years' duration. She states that the attacks start in the latter part of September. The condition is at its worst late in October. "As soon as the leaves are off the trees," as the patient states it, she feels all right. Please advise me what kind of agent could cause these attacks of asthma or hay fever. The physical examination revealed wheezing all over her chest.

M.D., Wisconsin.

ANSWER.—It is not uncommon to find patients who have asthma after the ragweed hay fever season is over. At this season one must think especially of corn smut or corn dust and of molds; perhaps the asthma coincides with fall house cleaning and the patient may be sensitive to house dust. Perhaps the patient may be allergic to fruits which are being preserved or she may be sensitive to foods eaten particularly at this season, e. g. grapes, pumpkin, plums and pears. It may be too that the dog or cat is invited into the house as cold weather sets in. In most cases careful history and thorough skin testing, both cutaneously and intracutaneously, will reveal sensitivity to one or more antigens.

ADDICTION TO AMPHETAMINE
(BENZEDRINE) SULFATE

To the Editor:—I wish to add my comments to the case reported on addiction to amphetamine (benzedrine) sulfate by Dr. L. J. Mahne in *Queries and Minor Notes*, November 2. First, his case is exceptional. I have used amphetamine (benzedrine) sulfate regularly in the treatment of alcoholism. I have run across no case in which the individual did not easily drop the drug after the desired results of prolonged abstinence from alcohol had been reached. The reason there have been no specific reports of cases of addiction to amphetamine sulfate is a simple one. Practically speaking, there are no such cases. In a continuous experience with the drug over the past four years I have not had one case which could be properly classified as drug addiction. True, there have been people who have suffered from chronic depression to whom the drug gave some degree of relief, who have continually used it during the period of time of treatment. However, they have not found it necessary to increase the dose in order to obtain the desired effect and, in fact, in the majority of cases the dosage has rarely been more than from one to one and one-half tablets a day, and in a considerable number of cases less than 10 mg. or one tablet a day has been sufficient. The psychologic effect is obtained more readily, I believe, with the smaller dose than the larger one. One might as well speak of the continued use of insulin by a diabetic patient as drug addiction. During the period of diabetes he has to take insulin steadily and continuously. When his disease recedes, so that diet alone is sufficient, he does not take insulin. The same situation prevails in the vast, almost overwhelming, majority of persons using amphetamine sulfate. Cases of sudden death have been recorded following the use of this drug but not beyond the range of mere coincidence. You cannot use any drug, including sterile saline solution, in a large number of cases without sudden death following an injection. If enough people with chronic or severe illness are treated with anything, death will ensue in some coincidental relationship. It is true that the drug should not be used when there is hypertension, gastrointestinal atony or profound excitement. Its use should be dropped immediately when good results do not follow quickly. Taking its total physiologic reactions into account and comparing it with other potent drugs, such as strychnine, atropine and digitalis, amphetamine sulfate is a relatively safe drug to use.

Abraham Myerson, M.D., Boston State Hospital,
Dorchester Center, Mass.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, December 14, page 2107.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 17-19. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, Jan. 7. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Eclectic*. Little Rock, June 5-6. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, Jan. 29. *Written*. Los Angeles, Feb. 24-27. Sec., Dr. Charles B. Pinkham, 1020 N. St., Sacramento.

COLORADO: * Denver, Jan. 7-10. Applications must be on file not later than Dec. 23. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: * *Medical*. *Written*. Hartford, March 11-12. *Endorsement*. Hartford, March 25. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homopathic*. Derby, March 11-12. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: July 8-10. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * Washington, May 12-13. Sec., Commission on Licensure, Dr. George C. Rubland, 203 District Bldg., Washington.

FLORIDA: * Jacksonville, June 23-24. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 8-11. Sec., Dr. James A. Morgan, 48 Young Building, Honolulu.

IDaho: Boise, April 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 335 State Capitol Bldg., Boise.

ILLINOIS: *Written*. Chicago, Jan. 21-22. *Reciprocity*. Chicago, Jan. 23. Supt. of Registration, Dept. of Registration and Education, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 17-19. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, Citizens Trust Bldg., Fort Wayne.

MAINE: Portland, March 11-12. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MASSACHUSETTS: Boston, March 11-13. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: * Ann Arbor and Detroit, June 11-13. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: * Minneapolis, Jan. 21-23. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity*. Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: *Reciprocity*. Helena, March 31. *Written*. Helena, April 1. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: *Reciprocity with oral examination*, Feb. 3. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: Concord, March 13-14. Sec., Board of Registration in Medicine, Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, June 17-18. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 14-15. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 27-30. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, State Education Department, 315 Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Sec., Dr. G. M. Williamson, 41 1/2 S. Third St., Grand Forks.

OREGON: * Portland, Jan. 14-16. Exec. Sec., Miss Lorianne M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia, January 7-11. Acting Sec., Bureau of Professional Licensing, Miss Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, Jan. 2-3. Sec., Division of Examiners, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH DAKOTA: * Pierre, Jan. 21-22. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

WASHINGTON: * Seattle, Jan. 13-15. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

WEST VIRGINIA: Charleston, March 3. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: * Madison, Jan. 14-16. Applications must be on file not later than Jan. 2. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, Feb. 3-4. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: Feb. 8. Address State Board of Healing Arts, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, April 21-22. Sec., Commission on Licensure, Dr. George C. Rubland, 203 District Bldg., Washington.

FLORIDA: De Land, June 7. Applications must be on file not later than May 24. Sec., Prof. J. F. Conn, John B. Stetson University, De Land.

JOYA: Des Moines, Jan. 14. Dir., Division of Licensure and Registration, Mr. H. W. Grete, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor, Detroit and East Lansing, Feb. 14-15. Sec., Miss Flora E. Dube, East Lansing.

MINNESOTA: Minneapolis, Jan. 7-8. Sec., Dr. J. Charnley McKinley, University of Minnesota, 126 Millard Hall, Minneapolis.

NEBRASKA: Omaha, Jan. 14-15. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

OREGON: Portland, Feb. 15. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: Providence, Feb. 19. Sec., Division of Examiners, Rev. Nicholas H. Serroc, Providence College, Providence.

WASHINGTON: Seattle, Jan. 9-10. Sec., Department of Licenses, Mr. Nelson N. Vaughan, Olympia.

Oregon June Report

Miss Lorianne M. Conlee, executive secretary, Oregon State Board of Medical Examiners, reports the written examination for medical licensure held at Portland, June 18-20, 1940. The examination covered 11 subjects and included 80 questions. An average of 75 per cent was required to pass. Thirty-one candidates were examined, all of whom passed. Four physicians were licensed to practice medicine by reciprocity and 3 physicians so licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1940)	85.8	89.1
Rush Medical College.....	(1939)	83	92.1
State University of Iowa College of Medicine.....	(1939)		88.5
University of Louisville School of Medicine.....	(1939)		90.1
University of Minnesota Medical School.....	(1940)	82	84.3
St. Louis University School of Medicine.....	(1939)	81.3	83
University of Nebraska College of Medicine.....	(1939)		83.8
University of Oklahoma School of Medicine.....	(1939)	84.1	86.9
University of Oregon Medical School.....	(1939)		80.9
		82.5, 84.4, 85.6, 85.8, 85.9, 86.5, 86.6, 88.7, 89, 89.3, 89.9, 90.1, 90.6, 91.4, 91.5, 92.9	

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Detroit College of Medicine and Surgery.....	(1933)		Michigan
University of Oregon Medical School.....	(1938)		Minnesota,
(1939) Wyoming			
Osteopath *			Colorado

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists.....	(1940, 2)	N. B. M. Ex.	
Harvard Medical School.....	(1938)	N. B. M. Ex.	

* Licensed to practice surgery only.

West Virginia July Report

Dr. Arthur E. McClue, secretary, Public Health Council of West Virginia, reports the oral and written examination for medical licensure held at Huntington, July 1-3, 1940. The examination covered 11 subjects and included 110 questions. An average of 80 per cent was required to pass. Twenty-five candidates were examined, all of whom passed. Sixteen physicians were licensed to practice medicine by reciprocity and 1 physician so licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....		(1939)	85.9
Northwestern University Medical School.....		(1939)	88.7
Rush Medical College.....	(1937)	89.8, (1938)	87.1
University of Maryland School of Medicine and College of Physicians and Surgeons.....		(1939)	85.2, 86.5
Harvard Medical School.....		(1938)	87.9
St. Louis University School of Medicine.....		(1938)	87.6
Columbia University College of Physicians and Surgeons	(1935)	86.3, (1939)	86.3
University and Bellevue Hospital Medical College.....		(1901)	84.9
New York University College of Medicine.....		(1938)	88.5
Medico-Chirurgical College of Philadelphia.....		(1914)	86
Temple University School of Medicine.....		(1939)	86.5, 88.7
Medical College of Virginia.....		(1939)	85.1, 85.8, 87.1, 87.3, 87.5, 87.7, 87.9, 88.3
University of Virginia Department of Medicine.....		(1939)	85.3, 87.1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists.....	(1939)		Maryland
University of Georgia School of			Georgia
Northwestern University Medical			Indiana
Rush Medical College.....	(1937)		Minnesota
State University of Iowa College of Medicine.....	(1937)		Iowa
University of Louisville School of Medicine.....	(1937)		Kentucky
Wayne University College of Medicine.....	(1939)		Michigan
Long Island College of Medicine.....	(1936)		Dist. Colum.
Western Reserve University School of Medicine.....	(1936)		Ohio
Meharry Medical College.....	(1930)		Tennessee
Vanderbilt University School of Medicine.....	(1937)		Tennessee
Medical College of Virginia.....	(1927)		N. Carolina,
(1937), (1939, 2) Virginia, (1939) Maryland			

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad.	of
Temple University School of Medicine.....	(1935)		N. B. M. Ex.

Book Notices

Public Health Administration in the United States. By Wilson G. Smillie, A.B., M.D., Dr.P.H., Professor of Public Health and Preventive Medicine, Cornell University Medical College, New York City. Second edition. Cloth. Price, \$3.75. Pp. 553, with 31 illustrations. New York: Macmillan Company, 1940.

Since the first edition of this book appeared five years ago there have been some extraordinary developments in public health administration in the United States. Some of these have been associated with new scientific information, such as that regarding scarlet fever, measles, influenza, the venereal diseases and particularly pneumonia. The relationship of nutrition to the public health has become more clearly defined, and the modern health department is greatly concerned with the general nutritional state of the people. The Social Security Act of 1935 revolutionized our national health program and modified greatly the administration of public health procedures. Dr. Smillie has reflected these changes in the new edition of his book, and he discusses the consolidation of the gains that have been made and the possibilities for the future. There is no longer any necessity for discussion as to the place of the public health officer in modern civic organization. However, the exact position which he is to occupy in relation to other phases of the public health is still a matter of considerable debate. It is well to find Smillie saying "The United States Department of Agriculture has estimated that one third of our population cannot afford to purchase even a minimum adequate diet. In our opinion this is a highly exaggerated statement." Of particular importance is a chapter on the practicing physician and the public health department. This material should be in the mind of every practitioner. A concluding chapter on the national health program discusses the present trend toward new legislation. Dr. Smillie is convinced that the United States is not ready for a nationwide plan of sickness insurance. He points out that we are not a totalitarian nation, that nationwide philosophies must develop slowly and must win the approval of the people who are to be benefited. Neither does he feel that our present organization of public health is ideal. Evolution is going on, and Dr. Smillie suspects that administrative devices which have not yet been initiated will eventually supplant our present type of organization.

Office Clinical Chemistry: A Laboratory Guide for the Practitioner and Hospital. By Emanuel M. Abrahamson, B.S., Ph.D., M.D., Adjunct Attending Physician, the Jewish Hospital of Brooklyn, Brooklyn. Cloth. Price \$5. Pp. 245, with 39 illustrations. New York, Toronto & London: Oxford University Press, 1940.

This volume is designed to aid the clinician by selecting chemical methods for the examination of blood and urine which are suitable for office practice. It is not intended as a supplement or substitute for the existing treatises on laboratory procedures suitable to the large hospital laboratory with extensive equipment.

In general, the author has made an excellent selection of more than sixty established procedures adaptable for office practice. Many procedures have been modified so as to eliminate needless duplication of solutions of slightly different concentrations and apparatus of similar nature. A flow sheet of apparatus, reagents and order of procedure is graphically presented with each method in an attempt to simplify the technic. It is hoped that such an attempt at simplification will not mislead the clinician into the belief that preliminary training is not necessary in order to carry out accurately the various procedures. A knowledge of fundamentals is essential to recognize causes for inaccuracies.

While different workers in clinical laboratories may disagree with the author in certain of his selections and modifications of technics, it is obvious that in the main the selection has been wisely made with much thought toward simplification of procedures as far as is compatible with an accuracy sufficient for clinical interpretations.

To mention what might be regarded as a few deficiencies: The Kingsley method for albumin-globulin ratio is much simpler and more accurate than the one outlined. The newer sulfanilamide reagent N(1-naphthyl) ethylenediamine dihydrochloride gives a more rapid and stable color. Ordinary Exton's reagent for urinary albumin is generally used. Better calcium and phosphorus methods are available. Also, while ten pages is

devoted to the Van Slyke apparatus for determining alkali reserve, followed by a note that the method is hardly suitable for office practice, a more simple and adequate titration method is not given. It would seem simpler also to purchase congo red paper and Nessler's solution. On page 41, in describing the preparation of protein-free blood filtrate, the author refers to the flask holding ten times the volume of blood. This would seem insufficient. To mention only one other impression: It would seem that the schema for determining the type of urinary calculus is unnecessarily involved, since the clinician usually desires to know only the type of calculus; that is, whether it belongs to the phosphatic, oxalic, uric or urate group or whether it is the cystine type, which occasionally is encountered.

This volume should serve a need that has long been felt by physicians in office practice and should be of great value to the clinician who desires to obtain clinical laboratory data in selected cases.

Principles of Animal Biology. By Lancelot Hogben, F.R.S., Regius Professor of Natural History in the University of Aberdeen, Aberdeen. Cloth. Price, \$3.75. Pp. 415, with 151 illustrations by J. F. Horrablin. New York: W. W. Norton & Company, Inc., 1940.

This book, by the author of "Mathematics for the Million," lies somewhere between the semipopular book on science and the high school or college textbook. Its reading would be hard going for the average individual untrained in science and yet it is probably not complete or technical enough to serve as a textbook for a formal course although it would be excellent as collateral reading. There are a few errors: The sketch titled the human forearm shows the upper arm instead and is not good at that; the term ergosterol is twice misspelled; the statement that "an adequate minimum (vitamin A or carotin) seems to help resistance to diseases like colds and influenza" is not really warranted. Likewise the statement "The composition of what is now called vitamin E, present in cereal oils and green leaves, especially lettuce, is not yet known" scarcely does justice to the close approach which has been made to accurate knowledge of the structure of this vitamin. Also it would have been well if the statement that complete absence of this vitamin results in sterility from degeneration of testes in the male and resorption of early embryos in the female had been qualified by indicating that this result has been proved only in experimental rats.

The author has compressed a large amount of valuable information on science and has in the main expressed this information clearly. Nevertheless it does not seem to be a popularization that is likely to receive an extensive circulation nor is it quite suitable as a textbook. Perhaps its usefulness in future editions might be increased by some further thought on which of these purposes the book is designed to serve.

A Textbook of Medicine. By American Authors. Edited by Russell L. Cecil, A.B., M.D., Sc.D., Professor of Clinical Medicine, Cornell University Medical College, New York. Associate Editor for Diseases of the Nervous System: Foster Kennedy, M.D., F.R.S.E., Professor of Clinical Neurology, Cornell University Medical College, New York. Fifth edition. Cloth. Price, \$9.50. Pp. 1,744, with 173 illustrations. Philadelphia & London: W. B. Saunders Company, 1940.

Textbooks of medicine increase in size continuously with the advancement of medical knowledge. Thus the present edition of Cecil's Textbook is 130 pages larger than the preceding edition. It appears with a green cover, whereas the previous edition was in blue. The book has been entirely revised and completely reset. One hundred and thirty-one additional illustrations are provided. Unfortunately, the paper used for a volume of this size makes reproduction of half-tone illustrations somewhat difficult, and the reproductions, particularly of x-ray films and of skin conditions, are not of the best. In the present edition there are new articles on equine encephalomyelitis, moniliasis, toxoplasmosis, disseminated lupus erythematosus, chronic bromide poisoning, riboflavin deficiency, uveoparotid fever, regional ileitis, amaurotic family idiocy and gargoylism. There are also new treatises on some of the topics previously covered as the result of the development of new information or the appearance of new research. Dr. Foster Kennedy, associate editor for diseases of the nervous system, has revised some of the chapters in that field. Recent advances in bacteriology have caused the transfer of Carrion's disease to the section on Rickettsial diseases and gangosa to the section on spirochetal infections. This one volume system on the practice of medicine

has earned for itself a high place in its field. The methods of presentation, the excellent editorship, the quality of the bibliography, the publisher's contribution, the excellent arrangement and the index assure for this work a position of leadership.

The Anatomy of the Female Pelvis. By F. A. Maguire, C.M.G., D.S.O., M.D. Third edition. Cloth. Price, 10s. 6d. Pp. 162, with 35 illustrations. Sydney & London: Angus & Robertson, 1940.

It is only forty years ago that we in this country drew rather steadily on British teachers in matters of obstetrics and anatomy and to some extent in gynecology. In their writings we looked for and we continue to look for clarity, sanity and vocabulary. Here we have a fair condensation of the subject, illustrated for the first time in the three editions. To these illustrations there are so many references that one is inclined to scrutinize them. Simplification that adequately depicts essentials is an achievement. In a few of the drawings, as in those of the lymphatics, this is the case, but where diagrams or near diagrams run to crude coarse lines they have little place, particularly with vulvas, where a measure of delicacy may be expected. Nor may a pelvic floor or a tube range twice the average thickness, nor a sacrum carry six sections throughout. Then again certain clinical points hardly fit American practice. A diagnosis of uterine position by the "impulse" rather than through routine bimanual palpation or seizure of the organ is one instance. Another is the repeated warning to take pains to avoid visualizing the vulva unless there is very positive evidence during the course of the examination that it needs inspection, thus setting us back to the early days of the pride in his skill of that doctor who always inserted the catheter under the darkness of the sheet—with the price in cystitis consequent on this modest achievement. This good summary from Australia needs all of it brought up to its best to compete with more successful textbooks.

Taber's Cyclopedia Medical Dictionary Including a Digest of Medical Subjects: Medicine, Surgery, Nursing, Dietetics, Physical Therapy. By Clarence Wilbur Taber and Associates. Fabrikoid. Price, \$2.50; Thumb-indexed, \$3. Pp. 1,488, with 273 illustrations. Philadelphia: F. A. Davis Company, 1940.

This book represents an ambitious project as evidenced by the statement on the title page that it includes a digest of medical subjects—medicine, surgery, nursing, dietetics and physical therapy. It does actually contain an enormous amount of information of value to the medical man besides its service as a dictionary; for example, a table of the clinically significant blood constituents, their normal and pathologic ranges, and a list of phrases and words in four foreign languages devised particularly for assisting a physician in obtaining a history. The book also lists the etiology, symptomatology, physical signs and treatment of diseases. This has led, however, to what is probably the major criticism: The opening two sentences under "Treatment of Diabetes Mellitus," for example, are not wholly acceptable. They read "X-ray applied to the adrenals and pituitary glands is being tried, rather successfully. This relieves the necessity for frequent hypodermic injections of insulin." Similarly the treatment described for arthritis is not really illuminating. It is a doubtful contribution to the best medical interests to include such brief and in some instances distorted discussions of etiology, prevention and treatment of disease in a work of this kind. Nevertheless the amount of information contained in the book is amazing and it will serve as a ready source book for a good deal of miscellaneous information and as a satisfactory medical dictionary. The editor has obtained the help of an excellent group of associates.

A fonocardiografia. Pelo Dr. Dante Pazzanese, chefe do serviço de cardiologia do hospital municipal de São Paulo. Paper. Pp. 160, with 90 illustrations. São Paulo: Prefeitura do município de São Paulo, 1940.

The number of publications dedicated to the subject of phonocardiography is on a steady increase. They deal with the technic of recording, description of new apparatus or interpretation of tracings. In view of the growing interest of the medical profession in heart sound recording there is a need for a comprehensive monograph on this subject. Thanks to his extensive experience, the author was well qualified to fill this gap and he accomplished his task in an enviable manner. After a succinct discussion of the diagnostic and didactic value of phonocardiography and a brief historical review, he describes the most

popular apparatus for heart sound recording and proceeds to analyze systematically the graphs in various cardiac lesions. Cambridge, Minot and Siemens recording apparatus were used by the author. To facilitate the interpretation of the tracings, simultaneous phlebograms or preferably electrocardiograms were made. There is no trace of loquacity, the style is simple, and reproductions of heart sound records are numerous and excellent. The book will prove invaluable to any physician interested in this newest method of examination of the heart.

Bibliography of Swimming. Compiled by Frances A. Greenwood, Department of Physical Education, University of Alabama, Tuscaloosa. Cloth. Price, \$4.25. Pp. 308. New York: H. W. Wilson Company, 1940.

This bibliography is a comprehensive survey of the literature on swimming, beginning with a book published in 1538 and including about 10,000 titles classified under 600 subjects, which range from those directly connected with swimming itself to material on air conditioning, poetry, pools and bathing places, spas and mineral baths, and water softening. References of special medical interest are found under such headings as Corrective Swimming and Underwater Gymnastics, Cripples, Diseases and Infections, Drowning, Physiologic Aspects, and Resuscitation. Author and subject entries, arranged in the same alphabet, are made for each item listed, with complete bibliographic data under the author and English translations of foreign titles under the subject. As a whole, the material seems well organized with a helpful division into specific subject headings and ample cross references to guide the user.

A Research Conference on the Cause and Prevention of Dental Caries. Chicago, Illinois, July First and Second, 1938. Cloth. Price, \$2. Pp. 178, with 4 illustrations. Chicago: The Good Teeth Council for Children, Inc., [n. d.].

This conference, held in July 1938, brought together representatives of eleven of the groups prominent in recent investigations in the field of dental caries from all over the United States and Canada. The proceedings contain not only the original papers but also a complete record of the discussion, which was both generous and critical. It therefore presents quite accurately the status of caries research as of July 1938 and, except for recent work in connection with fluorine and dental decay, gives a fair picture of the situation now, approximately two years later. It should be read not only by those who are interested or engaged in such research but also by all those who are concerned actively or otherwise in the prevention and about the cause of dental caries. It was truly characterized by one of the participants as "one of the most interesting presentations" ever listened to, but the original papers and discussions must be read and studied to be appreciated and evaluated. Even the closing summary by Dr. E. V. McCollum fails to develop the conclusions of the investigators and the results of the efforts through discussion to reconcile contradictions.

The Chronicle of Crichton Royal (1833-1936) Being the Story of a Famous Mental Hospital During Its First Century, and Illustrating the Evolution of the Hospital Care and Treatment of Mental Invalids in Scotland. By Charles Cromhall Easterbrook, M.A., M.D., F.R.C.P.E. With foreword: Some Early Crichton Memories, by the late Sir James Crichton-Browne, M.D., LL.D., F.R.S. Cloth. Price, 25s. Pp. 663, with 103 illustrations. Dumfries, Scotland: Courler Press, 1940.

The Crichton Royal Institution was founded in 1833 on an original estate of 40 acres (later increased to over 800) near Dumfries, Scotland, to care for mental invalids of all kinds. This book constitutes a review of the work of this institution over the intervening years, its staff, its physical additions and many other items of historical interest.

Psychiatry for Nurses. By Louis J. Karnosh, B.S., Sc.D., M.D., Associate Clinical Professor of Nervous Diseases, School of Medicine, Western Reserve University, Cleveland, and Edith B. Gage, R.N., Supervisor, Neuropsychiatric Division, City Hospital, Cleveland. Cloth. Price, \$2.75. Pp. 327, with 34 illustrations. St. Louis: C. V. Mosby Company, 1940.

This book presents psychiatry "with an eye to the peculiar needs of the nursing school of today." In its twenty-nine brief chapters it offers first a historical review of the subject, then the structure and mechanism of the personality, taking up the classification of mental diseases and the examination and management of patients. More detailed consideration is given in later

chapters to the specific types of mental disease and to an outline of the various therapies now in vogue. The practical approach to the psychiatric patient is ably described and the theoretical aspects of psychiatry are brought into clear view. Brevity may account for certain omissions and may permit certain biased statements to creep in. For example, there is disapproval of psychoanalytic therapy without the credit given for the value of psychoanalysis as a key to psychiatric knowledge. Again, in the discussion on the treatment of epilepsy, large doses of bromides are featured without mention of acne and other complications. In the main, the authors have succeeded in preparing a readable book, brief, lucid and interesting. Questions at the end of each chapter, a glossary and an index add to its usefulness.

An Introduction to Pharmacology and Therapeutics. By J. A. Gunn, M.A., M.D., D.Sc., Professor of Therapeutics and Director of the Nuffield Institute for Medical Research, University of Oxford, Oxford. Sixth edition. Cloth. Price, \$1.75; 6s. Pp. 242. New York & London: Oxford University Press, 1940.

Like its predecessors, the present edition of this well known little book provides the prospective student of pharmacology with a satisfactory didactic survey of the subject. The fact that six editions have appeared in ten years would seem to indicate that British students are well pleased with this method of approaching their course in experimental pharmacology. Doubtless the author requires supplementary reading of the more exhaustive textbooks in his own classes, as indeed he indicated in the preface to the first edition of this work; one would think, however, that there might be some danger of the lackadaisical type of student being satisfied with the preliminary sketch and never going on to a study of the larger canvas.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Libel: Publication Exposing Quackery Privileged Under State Statute.—In an article published in *Hygeia* entitled "Modern Medical Charlatans," the defendant, among other things, accused the plaintiff, John R. Brinkley, of being the apotheosis of quackery and of having made as much as \$55,000 a week "from his various quackeries." The plaintiff later brought suit in the district court of the United States for the western district of Texas to recover actual and punitive damages for libel. The defendant pleaded the truth of the statements of fact in the article and that matters of opinion contained therein were based on facts and were his reasonable and honest opinions and so were privileged within the meaning of the Texas statute which declares that reasonable and fair comment or criticism of matters of public concern published for general information shall not be made the basis of an action for libel. The proceedings of the trial were published in J. A. M. A. 112:1952 [May 13], 2050 [May 20], 2138 [May 27] and 2280 [June 3] 1939. Judgment was rendered for the defendant and the plaintiff appealed to the United States circuit court of appeals, fifth circuit.

Under the statutory law of Texas, said the circuit court of appeals, the truth of statements in publications is a defense to an action for libel even though the words are actionable per se. The testimony of the plaintiff tended to show the truth of the statements of fact complained of and there was no substantial evidence tending to show that the defendant was actuated by malice or that the plaintiff suffered any actual damage compensable in money. There remains to be considered, continued the court, but one more question—whether the expressions of opinion in the defendant's article were privileged under the laws of Texas. The gist of the defendant's article was that the plaintiff is a charlatan and a quack. According to the Century Dictionary, said the court, a "charlatan" is defined as "one who pretends to more knowledge or skill than he possesses, especially in medicine; a quack." A "quack" is defined as "an ignorant or fraudulent pretender to medical skill," and an

element of quackery is "to advertise or urge, as a quack does his remedies." With respect to the plaintiff's professional qualifications and activities, continued the court, the admissions in his testimony tended to show:

that he obtained his medical degree from an institution known as a diploma mill; that he had been practising medicine since 1915; that he began practising medicine in Milford, Kansas, in 1917; that he advertised, by pamphlets and newspapers and by radio broadcasting from his own station, an operation for transplanting goat glands in men for the purpose of sexual rejuvenation; that he had treated between 5,000 and 6,000 persons and he charged some of them nothing and some of them \$750 for the operation; that his gross income was about \$100,000 per month; that he abandoned this practice in 1933; that his license to practice medicine in Kansas was revoked in 1930 and his radio license was revoked by the Federal Communications Commission in 1930; that a license he had obtained to practice medicine in Connecticut was revoked; that he was indicted in California for a conspiracy to unlawfully practice medicine; that at the time the article was written he was advertising, by radio broadcasting from a Mexican station, his skill in treating prostatic troubles; that he would prescribe by letter for persons who wrote to him describing their symptoms, for which he charged \$2.

All learned professions have their standards of ethics. A lawyer who advertises and gives advice by mail without seeing his client would certainly be considered a shyster. There was no doubt whatever that the plaintiff by his methods had violated accepted standards of medical ethics. In the judgment of the court, the facts quoted above were sufficient to support a reasonable and honest opinion that the plaintiff was a charlatan and a quack in the ordinary, well understood meaning of those words. The information contained in the defendant's article, concluded the court, was a matter of public concern and, since the article was published for general information, the published statements complained of were privileged. Accordingly the circuit court of appeals affirmed the judgment for the defendant. A petition by the plaintiff for a writ of certiorari was denied by the Supreme Court of the United States.—*Brinkley v. Fishbein*, 110 F. (2d) 62; 61 Sup. Ct. 34.

Libel: Baker Hospital Not a "Public Institution."—Defendant Norman Baker, the founder and owner of the Baker Hospital at Eureka Springs, Ark., in June 1939 wrote an open letter to Mr. and Mrs. Ray Freeman, residents of Eureka Springs, and to the Eureka Springs Boosters' Association and caused it to be published in a local newspaper, the *Daily Times Echo*. Mr. Freeman was a city official, a member of the Eureka Springs Boosters' Association and of the chamber of commerce and was financially interested in a wholesale grocery store, a swimming pool and a tourist camp. In this letter Baker used language tending to impeach the honesty, integrity, veracity and reputation of the Freemans. He accused them of making unfavorable comments about the Baker Hospital to persons who stopped at their tourist camp, persons who would otherwise have become patients of his hospital and would have spent a large amount of money in the city. He pointed out that all the local merchants would make more money if the Freemans desisted from actions which "are tearing down the good the Baker Hospital is doing." He said that the Freemans advised their patrons at the tourist camp to investigate about town before going to the Baker Hospital because it was a horrible and unfit place and had no licensed doctors. Finally he recommended that the boosters' association and the chamber of commerce expel Mr. Freeman from membership in their respective organizations and further that they sponsor a movement to oust or remove Mr. Freeman from city office. In conclusion he wrote:

Can the citizens expect the Baker Hospital and other progressive citizens to give good co-operation as long as these ungentlemanly, underhanded and contemptible things exist?

On the basis of this letter, which the jury found contained false and untrue statements, the defendant was convicted of criminal libel in that he unlawfully, wilfully, maliciously and falsely exposed the Freemans to public hatred, contempt and ridicule. From this conviction Baker appealed to the Supreme Court of Arkansas.

Baker attempted to justify his remarks on the ground that the open letter was a privileged communication. His theory was that the Baker Hospital was a public establishment depending on the public for support and that therefore he had the right to defend that institution from unjust and malicious attack, as contained in false or untrue statements. The Supreme

Court, however, held that the Baker Hospital was not a "public institution" but was a purely private enterprise, and that it depended on public support only in the same manner and degree as does any other community enterprise, be it a department store, barber shop or meat market. There was nothing in the record to indicate that the Baker Hospital was an organized charity conducted in the public interest. Furthermore, said the court, in the first paragraph of the published letter the defendant assumed full responsibility for the statements contained therein and attempted to absolve the Baker Hospital from any blame that might follow from the publication when he stated: "It is understood that I write this personally, without any connection with the Baker Hospital, but as an honest and progressive citizen, interested in the welfare and upbuilding of the community." In the judgment of the court, this statement conclusively showed that the communication was not a privileged one and was not so regarded by the defendant himself. Accordingly, the Supreme Court of Arkansas affirmed the judgment of conviction of libel. Baker then petitioned for a writ of certiorari to the United States Supreme Court, but his petition was denied.—*Baker v. State (Ark.)*, 137 S. IV. (2d) 938; 61 Sup. Ct. 25.

Society Proceedings

COMING MEETINGS

- American Student Health Association, Ann Arbor, Mich., Dec. 27-28. Dr. Ralph I. Canuteson, University of Kansas, Lawrence, Kan., Secretary.
- Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otolological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.
- Middle Section, American Laryngological, Rhinological and Otolological Society, Chicago, Jan. 27. Dr. Walter H. Theobald, 307 North Michigan Blvd., Chicago, Chairman.
- Society of American Bacteriologists, St. Louis, Dec. 27-29. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
- Society of Surgeons of New Jersey, Newark, Jan. 29. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.
- Southern Section, American Laryngological, Rhinological and Otolological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.
- Western Section, American Laryngological, Rhinological and Otolological Society, San Francisco, Feb. 1-2. Dr. Robert C. Martin, 384 Post St., San Francisco, Chairman.

THE AMERICAN RHEUMATISM ASSOCIATION

Seventh Annual Meeting, held in New York, June 10, 1940

DR. LORING T. SWAIM, Boston, Secretary

(Concluded from page 2116)

An Oft Recurring Disease of Joints (Arthritis, Periarthritis, Para-Arthritis) Apparently Producing No Articular Residues

DR. PHILIP S. HENCH, Rochester, Minn.: The outstanding features of an unusual articular disease are multiple afebrile attacks of acute arthritis and periarthritis, sometimes also para-arthritis, with pain, swelling, redness and disability generally of only one but sometimes of more than one small or large joint of adults of either sex. The attacks appear suddenly, develop rapidly, generally last only a few hours or days and then disappear completely, only to recur at short or long irregularly spaced intervals. Despite the (transitory) presence of an acute or subacute inflammatory reaction in joint tissues and a fibrinopurulent exudate in the articular cavity (in some cases) there is little or no constitutional reaction or abnormality in laboratory tests, and no significant functional, pathologic or roentgenographic residues occur even after years of disease and scores or even hundreds of attacks.

Of the thirty-four patients nineteen were females, fifteen males. At the onset of the disease the patients were from 13 to 68 years of age (70 per cent were from 20 to 39). The disease had lasted from three months to twenty-five years, a total of 242 (average seven) years. Attacks had occurred at the rate

of from two to ten yearly in nine cases, from twenty to sixty a year in seventeen cases, from 100 to 200 a year in three cases, and 250 or more a year in five cases; in the latter cases some joint or other was involved almost daily in a short attack, but successive attacks were not necessarily in the same joint. Four patients had each had "hundreds" of attacks; the remaining thirty patients had had a total of at least 4,930 attacks, an average of at least 164 attacks per patient within the average of seven years of illness, or twenty-three attacks per patient yearly.

The attacks lasted usually from one to three days, rarely more than one week. The intervals between attacks varied from only one or two days in those most frequently affected to one or six months in others. In 90 per cent of cases attacks were usually monarticular; occasionally two or more joints were simultaneously involved. Favorite sites were a finger joint, wrist, shoulder, knee, toe or elbow but practically any joint was liable to attack. Attacks appeared suddenly and progressed rapidly. Pain was sometimes mild, generally a severe ache, occasionally severe enough to require narcotics. Disability was considerable, producing temporary loss of function of the affected joint. Some patients were often forced to go to bed.

Red, tender, painful para-articular swellings occasionally appeared in 30 per cent of the cases at characteristic sites; they lasted only six to twenty-four hours; they differed from angioneurotic edema. In three cases intracutaneous or subcutaneous nodules also occurred occasionally, generally on the fingers.

There was little or no constitutional reaction, no fever in any attacks observed, no loss of appetite, generally no weight loss. Anemia was absent in 94 per cent. Total white counts were generally normal, but a relative lymphocytosis without eosinophilia was generally present. Sedimentation rates were generally normal between attacks and generally but not always slightly elevated during attacks (the average of thirty-three tests was 24 mm.). A moderate lipemia was present. Of the 164 roentgenograms of joints made, 150 (91 per cent) were entirely negative; the rest revealed coincident unrelated disease (bunions, hypertrophic changes in elderly patients).

Biopsies made during attacks (three cases) revealed an acute or subacute inflammation in synovial membrane and capsule, sometimes in tendon sheaths, and a fibrinopurulent exudate in the joint cavity. A biopsy of a knee between attacks revealed no gross or microscopic abnormalities.

The cause of the disease was not determined. The evidence collected against an allergic hypothesis outweighed that for it. Cultures of biopsy material were negative. Differentiation of this condition from atrophic arthritis, intermittent hydrarthrosis and gout was made. The cases possessed many of the features of the "angioneural arthrosis (periarthrosis, parathyrosis)" of Solis-Cohen (1913) or of Kahlmeter's (1939) "allergic articular and periarticular rheumatism," but certain differences were described.

Treatment included epinephrine, ephedrine, benzedrine, ergotamine tartrate, removal of foci, autogenous vaccines, low purine diets, diets free of suspected foods, histaminase, histamine desensitization and typhoid vaccine reactions. None of these methods gave impressive results. Follow-up data on twenty-seven cases were reported. A cure (spontaneous?) had occurred in four cases (15 per cent), slight improvement in twelve cases (44 per cent) and no change in seven cases (27 per cent); three patients (11 per cent) were having more frequent (but not longer) attacks. One patient died of coronary disease. There appeared to be no tendency for the disease to become chronic in a given joint. Despite the thousands of attacks suffered during a grand total of 307 years of illness (242 prior to plus sixty-five years since admission) no permanent crippling had affected any joint.

DISCUSSION

DR. K. K. SHERWOOD, Seattle: No matter how detailed and clearcut the description of a syndrome of arthritis is, it warrants reemphasis that this syndrome portrays a variant from the ordinary forms of chronic infectious arthritis both as to etiology and as to cause and is not a new disease but a variation. With this reservation I feel that the splitting of chronic arthritis not only into the hypertrophic and atrophic group but into smaller

subdivisions of clinical syndromes is of great value prognostically and therapeutically. This description may be held as a classic example of how each individual syndrome of chronic arthritis should be described and isolated if it is to be considered as a variant. Several years ago Dr. Hench described the occasional startling remissions occurring in chronic infectious arthritis with the onset of jaundice. Essentially each of these attacks resembled a case of chronic infectious arthritis of hours' duration rather than of months' duration. I have observed early cases of atrophic arthritis in which the joint symptoms preceded the constitutional manifestations of the disease and feel, therefore, that this syndrome might be regarded as an abortive form of true infectious or atrophic arthritis. It would seem worthy of detailed investigation in the cases described by Dr. Hench to determine whether or not a factor of abnormal liver metabolism might not be the reason for the nonprogression of these cases. A detailed study of the liver function in these cases might be of value in aiding one in learning why jaundice occasionally is of such dramatic therapeutic value.

DR. RUSSELL L. CECIL, New York: I cannot recall having seen a case exactly like the cases described, though I am sure we have all had the experience from time to time of seeing cases of joint swelling which we could not classify. I recall several in which I suspected an angioneurotic phenomenon. I am not referring to classic intermittent hydrops. I have seen several of the latter develop typical rheumatoid arthritis. Dr. Hench's cases should not be confused with intermittent hydrops, and the disease should not be called rheumatoid arthritis because of the lack of constitutional reaction and the failure of the disease to make any permanent changes in the joint. There is no progress toward chronicity and no injury to the synovial membrane. It seems that Solis-Cohen looked on this condition as an angioneurotic phenomenon, while Kahlmeter leaned more toward the allergic point of view. Dr. Hench has shown in his pictures that an actual leukocytic exudate was present in more than one case. It would hardly be fair, therefore, to call such a condition a purely angioneurotic state. I believe that the hypersensitive joint is something we are just beginning to understand.

DR. RALPH K. GHORMLEY, Rochester, Minn.: It has been my privilege to see a few of these patients from time to time with Dr. Hench, and I wish to corroborate as far as I am able the statements he has made and the facts he has presented, particularly as far as the pathologic changes are concerned. I have examined these tissues and they do not present a picture of infectious arthritis. The leukocytic exudation is more striking in some of the specimens than in those he showed on the screen.

DR. WALTER BAUER, Boston: It is too soon to say that the thirty-four patients described by Dr. Hench are suffering from one and the same disease. I myself believe that follow-up studies will show that he has included a number of diseases. On the other hand, it must be realized that from 5,000 to 6,000 cases of joint diseases are seen at the Mayo Clinic each year. Therefore it is conceivable that he has gradually weeded out thirty-four patients suffering from a rare disease or syndrome. His figures are not as impressive as they would appear at first glance, 642 years of the disease without any residual of joint changes. If one scrutinizes his analysis, one finds that five patients had the disease less than one year and another ten less than five years. I believe it is impossible to say what these fifteen patients are suffering from. The pathologic changes described could fit any number of acute diseases involving articular tissue. Oft repeated sedimentation rates, leukocyte counts and rectal temperatures on all these patients would be of considerable diagnostic help. One must further realize that diseases may vary considerably in clinical pattern. The same disease in one patient may be extremely atypical and benign, and in another individual it may have a malignant course. This group may have included atypical examples of rheumatic fever, rheumatoid arthritis, gout and allergic diseases.

DR. J. ALBERT KEY, St. Louis: I think this is definitely a disease syndrome. One cannot expect them all to last fourteen years. I should like to know whether there was any preponderance of eosinophils in the sections. Any acute reaction that lasts

a few days will give a polymorphonuclear leukocytic exudate. I have seen one or two and thought they were allergic. They do resemble an abortive gout.

DR. PHILIP S. HENCH, Rochester, Minn.: There was no notable increase of eosinophils either in the circulating blood or in the sections of inflamed tissue removed for biopsy. When I use the term "new syndrome" I refer to one which is new to the consciousness of the general practitioner and even to the "rheumatism specialists" of today. The disease, of course, is not new, and Solis-Cohen and Kahlmeter may indeed have described the same disease. In describing a new syndrome it is difficult not to adulterate the series with cases which do not belong to it. It is therefore natural to suggest that I have fallen into such an error and included cases which in time will be recognized as somewhat atypical rheumatoid arthritis or rheumatic fever. However, I feel that I have already excluded such cases; I discarded a few cases that at first resembled those of the series in some degree but in which within a few months to two or three years the patients began to have longer and longer attacks, which finally became continuous. But there remains a group of thirty-four patients observed over a total period of 307 years, almost ten years each, who present the characteristic and unusual clinical picture which I have described. Do we have the right to consider them to have atypical atrophic arthritis and then wait for the permanent residual intra-articular changes of atrophic arthritis to show themselves? We must be open minded; we must not give a new name to every variety of one disease, but at the same time we must be ready to recognize a new syndrome when faced with it clearly and repeatedly. However, three of these patients were physicians, one a distinguished orthopedic surgeon. Having studied their own disease long and intensively, to them the diagnosis of atrophic arthritis or any other recognized syndrome had long since become quite untenable. We are now seeing seven to nine cases a year and the condition may be commoner than is now apparent. We shall certainly follow our cases closely and I hope to report again concerning them at a later date.

The End Results of Synovectomy of the Knee Joint

DRS. R. K. GHORMLEY and D. M. CAMERON, Rochester, Minn.: A review of the end results in cases in which synovectomy has been performed at the Mayo Clinic reveals the fact that synovectomy has been performed 103 times on eighty-eight patients. Of these, fourteen underwent bilateral synovectomy and one underwent synovectomy of an ankle in addition to synovectomy of both knees. Without resorting to argument as to the feasibility of synovectomy for other joints, we believe that it is a procedure most adaptable to the knee joint, and that other joints can be left out of consideration in this abstract. The operations were performed for chronic synovitis, chronic infectious arthritis, traumatic arthritis, synovial osteochondromatosis, xanthoma of the synovial membrane, intermittent hydrops, tuberculosis, hypertrophic arthritis and chronic synovitis which later developed into polyarthritic involvement, but which in all probability was chronic infectious arthritis at the onset. Of the patients undergoing this operation, end result studies show that three are dead (one from operative shock), and the end results are known in ninety cases in which operation was performed. Of the ninety patients, 34.4 per cent are in excellent condition, 33.3 per cent are improved, and 32.2 per cent are in poor condition, at the time of writing. Studying the end results by groupings, it is found that all the patients with traumatic arthritis, osteochondromatosis, xanthoma and hypertrophic arthritis were either cured or improved. Of the patients who had chronic synovitis, 77.4 per cent were cured or improved, whereas 56.2 per cent of those who had chronic infectious arthritis were improved or cured and 54.9 per cent of those who had synovitis which later developed into chronic infectious arthritis were improved or cured.

DISCUSSION

DR. PAUL P. SWETT, Bloomfield, Conn.: By a slight rearrangement of the figures it is found that out of fifty-two cases of atrophic arthritis only twenty-four showed a combination of improved or excellent results. Thus the authors' figure of about 50 per cent improvement agrees with Dr. Inge's recently reported conclusion that synovectomy offers a chance of helping about

half of the cases of atrophic arthritis. This means that we are not yet able, after nearly twenty years' experience, to define the conditions under which synovectomy can be expected to yield a high percentage of good results. This is especially unfortunate because it is highly important to be able to give exact indications for any operation which might add to our resources for managing the great group of the chronic arthritides which is most in need of treatment and in which synovectomy sometimes yields brilliant results. To clarify this situation it may be said that the successful use of synovectomy must be based first on consideration of the type of the disease and second on the stage of the process. Under the type of the disease it must be remembered (1) that the operation is applicable only to a synovial proliferative process, (2) that, as was first shown by Nichols and Richardson and later confirmed by Allison and Ghormley, the characteristic pathologic change in atrophic arthritis is proliferation but, while this commonly first occurs in the synovia, it also occurs in the perichondrium, the endosteum and the epiphyseal connective tissue and (3) that, as has been emphasized by Pemberton and Osgood, there are two important variants of the disease in which either capsular fibrosis or muscular fibrosis is the predominant characteristic. Hence in the selection of the candidates for synovectomy it is necessary to exclude those cases in which the proliferative process is not primarily and predominantly synovial as well as those variant types which obviously are not suitable for this form of treatment. The stage of the process in which synovectomy may be most useful is (1) as soon as it can reasonably be determined that the proliferation is not going to undergo spontaneous resolution, (2) before the proliferation has caused irrevocable damage to the joint structures and (3) before protracted invalidism has so depleted the patient that no form of treatment can any longer be helpful. It is probable that the failures of synovectomy are to be found among those cases in which the disease was not primarily and predominantly synovial or in those instances in which the operation was done too late. Further reports on this work should be based on a series of observations in which the conditions outlined have been fulfilled.

DR. FRANK D. DICKSON, Kansas City, Mo.: It has been my experience over the last twenty years in some 140 synovectomies that proper removal of the synovia and other material in an infected joint results in a large percentage of cases in improvement in other joints. It is something that happens far too often in my experience to be ignored. I believe that many failures in synovectomy are traceable to an incomplete operation. If one simply removes the synovia and leaves behind disintegrated semilunar cartilages and joint cartilage which is partly or largely destroyed by pannus, and projecting hypertrophic margins, one cannot expect a good result. Synovectomy to be successful must be complete, and this in the knee always includes removal of the semilunar cartilages, removal of all cartilage destroyed or partly destroyed by pannus, removal of all hypertrophic osteophytes, and reducing the joint surface to an area represented by the cartilage which was considered satisfactory enough to be allowed to remain in place. If more thorough, more complete, operations were done the results would be better. Only a few months ago I did a complete synovectomy on a right knee and a partial one on the left. The patient came back after two months with the right knee in excellent condition but the left knee about as bad as it had been before. I then operated on the left knee again and did what ought to have been done in the first place, a complete synovectomy, with later a satisfactory result on the left knee also. I believe the result obtained by synovectomy is entirely dependent on the thoroughness of the operation performed.

DR. J. ALBERT KEY, St. Louis: I have seen some of Dr. Dickson's cases and I am convinced that he is right. By doing a radical synovectomy in some of these early cases of presumable rheumatoid arthritis in which the principal disease is in one or both knee joints, his results are good. In intermittent hydrarthrosis this is the operation of choice even though it does not always cure.

DR. RALPH K. GHORMLEY, Rochester, Minn.: I agree with Dr. Swett that the selection of the cases is the important thing. We have tried to select cases only when the synovial membrane was involved and the articular surfaces were intact. Dr. Dick-

son's cases were more advanced. It seemed to me that he has opened up a further indication for this operation by doing a more complete operation. It is helpful to put on casts for ten days and then start movement—passive movement at first, then later active movement. Later, manipulation for three or four weeks may be helpful.

Experiences with Roentgen Therapy in Various Rheumatic Conditions

DRS. C. J. SMYTH, R. H. FREYBERG and W. S. PECK, Ann Arbor, Mich.: One hundred patients, the majority of whom had characteristic rheumatoid arthritis, others having rhizomelic spondylitis, degenerative joint disease or so-called fibrositis, were given roentgen therapy to some of the joints. For the most part, patients were selected having pairs of comparably affected joints and in such cases roentgen treatment was applied to only one of the pair, the other untreated joint serving as a control. In still other cases the possible psychic effect of such treatment was studied by screening some joints with lead so that no x-rays reached the skin. The effect of such treatment was measured by careful study of the subjective response, physical changes at the joints, frequent erythrocyte sedimentation rate determinations, diagnostic x-ray examinations of the joints, changes in joint fluid from both treated and untreated joints before and after roentgen therapy and in several cases by microscopic study of joint capsule and synovial biopsies. The results of treatment are analyzed in regard to the type of disease, the duration of illness, activity and extent of the disease.

DISCUSSION

DR. W. PAUL HOLBROOK, Tucson, Ariz.: Last year Dr. Freyberg discussed sulfur therapy and buried it thoroughly. This year it is roentgen therapy. It will take Dr. Freyberg only a few years to dispose of all our therapeutic agents at the rate he is going. This is a carefully controlled experiment with roentgen therapy. A few years ago Dr. Kahlmeter reported on the subject and I have done a little work with it. Dr. Kahlmeter's cases were certainly not controlled as Dr. Freyberg's have been. My experiences, though small, have been identical with those obtained by Dr. Freyberg in rheumatoid arthritis. I have experienced two differences. First I have had better luck in the control of pain about the shoulder from bursitis with roentgen treatment than Dr. Freyberg indicated. Whether it has anything to do with curing the disease or not I do not know, but if the pain can be controlled it is helpful. Second, I have had no such brilliant results with spondylitis as Dr. Freyberg reports.

DR. LORING T. SWAIN, Boston: This paper represents the beginning of the best controlled study of roentgen therapy to date. The estimate of the results in arthritis is difficult because of the nature of the disease and the psychologic effects of any and all forms of treatment. It is a purely local form of treatment and should not be expected to affect the constitutional disease. No changes have been found in the sedimentation rate; the x-rays cause no beneficial change in the bones or joints. I believe the effect is in the soft tissues and that they appeared gradually less swollen and that ultimately the growing villus tissue in the joints decreased. I believe the chief value is in decrease of pain due to hyperemia in the soft tissues. Spasm is consequently less and motion increases. My colleagues and I were not particularly impressed with the psychologic effect of roentgen treatment in our cases and therefore did not use a lead screen. This is a valuable addition to methods of control. We have treated one of two joints in many cases, but this does not give an adequate control of the mental factors. We have not stopped other treatments, but in certain cases merely added roentgen treatments.

Roentgen treatment was begun at the Robert B. Brigham Hospital in 1932 of one child whose left knee had been operated on for synovial overgrowth with poor results. X-rays have given her an excellent right knee, eight years later. Up to March 1940 we have completed treatment of 164 patients. Of these eighty-five were for rheumatoid arthritis, thirty-one for osteo-arthritis, twenty-eight for a combination of osteo-arthritis and rheumatoid arthritis and eighteen for Strümpell-Marie arthritis. Treatment was first given for relief of pain, but it

was soon observed that swelling and limitation of motion decreased gradually under roentgen treatment. We have listed the end results according to subjective improvement and objective improvement. By subjective improvement we mean relief of pain and stiffness. By objective improvement we have listed measurable decrease in swelling and measurable improvement in motion. There were no observable roentgenologic changes except that recalcification of the bone was observed somewhat more frequently in patients receiving roentgen treatment in comparison to those not receiving roentgen treatment; this has been mentioned in medical literature. No complications or untoward reactions were observed. In the patients with rheumatoid arthritis, subjective improvement was observed in over 90 per cent of those in whom the swelling and pain in the joints had been of six months duration or less. There was also objective improvement. Of the patients whose arthritis was from six months to two years in duration subjective improvement was observed in about 85 per cent and objective improvement in 60 per cent. Of the patients whose arthritis was of long duration, over two years, subjective improvement was observed in about 72 per cent and objective improvement in 52 per cent. Of the patients with osteo-arthritis there was no appreciable difference between the early, moderately advanced and late cases. These were improved subjectively in 70 per cent and objectively improved in 45 per cent. Of those patients who had evidence of both rheumatoid arthritis and osteo-arthritis there was subjective improvement in only 63 per cent and objective improvement in 25 per cent. In Strümpell-Marie arthritis relief of pain in the back was observed in only three cases. Pain in the hip or shoulder joint was relieved in 50 per cent of the patients; objective improvement was observed in about 15 per cent.

In rheumatoid arthritis, the earlier the case is treated the more rapid is the response. Children seem to respond more quickly to this form of treatment than adults. Frequent small doses continued for a long period of time give better results than larger doses given at longer intervals or for only a few times. In the Strümpell-Marie arthritis improvement was noticed only when twelve or more treatments had been given at fairly frequent intervals—two weeks or less. Improvement was usually observed only after the lapse of a year. Treatment was of three types: For small joints (knee joint or smaller) the following formula was used: 118 kilovolt peak, 5 milliamperes, 1 mm. of aluminum filter, 90 roentgens per minute, two and one-half min. = 225 roentgens, 14 inches distance. For spines, 130 kilovolt peak, 5 milliamperes, 3½ mm. of aluminum filter, 39 roentgens per minute, 5 minutes = 195 roentgens, 14 inches distance. For osteo-arthritis of the knees and hips, 130 kilovolt peak, 5 milliamperes, 3 mm. of aluminum filter, 39 roentgens per minute, 2¾ minutes = 107¼ roentgens, 14 inches distance. These formulas were gradually developed after several years of trial and seemed to be the best in our experience for the conditions listed. Treatments were given on the average of once every two weeks. The formula we believe is important.

I would ask Dr. Freyberg to reserve judgment about his results both objective and subjective until from three to five years has elapsed. Our belief is that early, adequate roentgen treatment of rheumatoid arthritis is helpful locally. It relieves pain in osteo-arthritis, and has helped hips in Strümpell-Marie spondylitis.

DR. EUGENE T. LEDDY, Rochester, Minn.: Most of the cases of arthritis referred to the radiologist for treatment are in the group for which little can be done, and one in which the results of treatment are in no sense outstanding. The technic of the roentgen treatment of arthritis is by no means standardized and is largely a matter of choice of the radiologist. Most of us have a few fairly definite rules which we modify to fit the individual case. My own view is that, since arthritis is a chronic inflammatory disease, the use of both high voltage and high doses is unnecessary. I therefore feel that the technic described by Dr. Freyberg is too intensive. In general, the earlier the stage of arthritis the better is the result, and I think that the more acute the case, the lower should be the dose of x-rays used in its treatment. There is one type of arthritis which I think is unfavorable for roentgen treatment, and that is the group in which there has been deposition of bone. I know of no radiologic technic which will cause dissolution of these bony deposits. However, roentgen

treatment is worth a trial in this group for its possible pain-relieving effect. In many cases of arthritis, relief of pain follows roentgen treatment without there being any changes demonstrable in the roentgenogram to account for it. The explanation of the effect of roentgen treatment on arthritis is somewhat controversial, but I feel that it is largely destruction of leukocytes in the inflammatory process.

DR. ERNST FREUND, Boston: In rheumatoid arthritis as well as in other chronic diseases it is helpful to have a treatment which gives a symptomatic result. In some cases in which inflammation is present the results are better if one first removes the effusion by puncture or by physical or medical means. One of the first indications of periarticular disease is involvement of the shoulder, followed by the hip and knee. In some the results obtained by x-rays are better than with other means. I have never treated women between the ages of 15 and 45 with x-rays for sciatica or sacro-iliac arthritis because I have seen some treatment given elsewhere which resulted in sterility. Some other diseases, such as superficial irritations of the periosteum, like epicondylitis and styloiditis, and similar conditions such as bursitis, respond well to roentgen treatment. I have had relatively good results with this kind of treatment.

DR. JOSEPH A. FREIBERG, Cincinnati: I myself have seen no harmful effects of roentgen therapy but I do not think it should be given in this condition, especially since Dr. Freyberg mentioned that in several of his cases there was an increase in osteoporosis following therapy. Whether he attributed the osteoporosis to the therapy I was not quite certain. We attempt to increase the blood supply, and if high voltage roentgen therapy or any similar treatment is used we may lessen the blood supply to the joint subsequently. I do feel that roentgen therapy is used rather promiscuously in some instances about joints. I have seen extensive osteoporosis following high voltage therapy. I think it would be questionable to use roentgen therapy in arthritis unless it has some very definite effect which cannot be obtained by other means.

DR. R. H. FREYBERG, Ann Arbor, Mich.: I am not a therapeutic nihilist, but I do think that an appraisal of all forms of therapy should be made under controlled conditions and with no undue enthusiasm. Dr. Holbrook mentioned that the results of treatment of spondylitis in his group of patients had not been as brilliant as ours. I do not think our results should be considered brilliant. I contrasted them with results in patients with rheumatoid arthritis, among whom I think they were distinctly poor. We have been encouraged to continue to use roentgen therapy in spondylitis. Diagnosis in the earlier stage of rhizomelic spondylitis is difficult. It is obvious that late in the course of the disease one cannot expect cures from any therapy. If one is going to help these patients one must use treatment of value in the early stage. The patients in whom we observed the best results were those seen early in the stage of development of signs and symptoms characteristic of rhizomelic spondylitis; there was no demonstrable calcification of the paraspinal ligaments; the erythrocyte sedimentation rate was elevated. We have followed our patients, with few exceptions, for at least six months; 50 per cent were observed for more than twelve months, and many for more than eighteen months after treatment. We think this is long enough to get an idea of what effect x-rays will have. We have had no experience in treating younger individuals as Dr. Swaim has. Our patients have always been adults. The technic of irradiation may explain the results that Dr. Swaim mentioned in contrast to ours, though we think it quite unlikely. The development of technic in treatment of rheumatic diseases so far as I can find is about as mysterious as the use of it at all. Dr. Swaim's technic differs from ours in that treatment was given more often and for a longer period. Dr. Freund mentioned getting better results when synovial fluid was removed from the joints later treated. We have observed no difference in aspirated and un aspirated joints. I am glad Dr. Freiberg raised the question about the ill effects. We have had no ill effects except nausea and vomiting lasting for only a few days during treatment. Depilation and pigmentation of the skin occurred in some cases. We saw one patient treated elsewhere who had cutaneous changes indicative of a roentgen dermatitis. I want to add my warning that one should keep in mind the possible harmful effects.

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Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

20:389-518 (Oct.) 1940

Morphologic Study of Cardiac Conduction System in Ungulates, Dog and Man: Part I. Sino-Atrial Node. D. J. Glomset and Anna T. A. Glomset, Des Moines, Iowa.—p. 389.

Mechanism and Nature of Ventricular Fibrillation. C. J. Wiggers, Cleveland.—p. 399.

*Physiologic Basis for Cardiac Resuscitation from Ventricular Fibrillation: Method for Serial Defibrillation. C. J. Wiggers, Cleveland.—p. 413.

Estimation of Cardiopulmonary Functional Capacity by Means of Oxygen Debt Studies. F. C. Sutton, Cleveland; J. A. Britton, Chicago, and J. G. Carr, Evanston, Ill.—p. 423.

Combined Use of Ouabain and Digitalis in Treatment of Congestive Heart Failure. R. C. Batterman, O. A. Rose and A. C. DeGraff, New York.—p. 443.

*Rheumatic Heart Disease: Analysis of 796 Cases. B. J. Clawson, Minneapolis.—p. 454.

Diagnosis of Coronary Occlusion and Myocardial Infarction by Fluoroscopic Examination. A. M. Master, R. Gubner, S. Dack and H. L. Jaffe, New York.—p. 475.

Effects of Whole Bile and Bile Salts on Innervated and Denervated Heart. K. G. Wakim, H. E. Essex and F. C. Mann, Rochester, Minn.—p. 486.

Cardiac Resuscitation from Ventricular Fibrillation.—

Wiggers points out that the high incidence of death from ventricular fibrillation secondary to coronary occlusion and accidental electrocution from electrical appliances make ventricular fibrillation of special interest. The author's experience has convinced him that the physiologic basis for resuscitation rests on the conception that ventricular fibrillation is not a constant phenomenon but an evolving series of changes from the moment of its inception until its cessation, which consumes from thirty to forty-five minutes. Asynchronicity and incoordination involve progressively smaller blocks of myocardium, in which the character of the contraction alters as anoxia progresses because of the cessation of coronary flow. Consequently, restorative procedures must recognize the state which exists at the time the procedures are applied. For example, the atonic stage of fibrillation, in which anoxia causes depression of contractile force and slows conduction, develops in from two to five minutes after the onset of fibrillation. Although fibrillation can be readily stopped at this time, the coordinated beats which redevelop are exceedingly weak and dynamically useless. Consequently, one of the problems of revival consists in finding a means which can be employed within the first three minutes or in devising expedients for more forceful beats. The use of powerful stimulants, such as epinephrine and related substances, must necessarily prove valueless because they cannot substitute for oxygen lack. The author, as well as Wegria, has had success in his experimental work with a modification of the countershock method, which he calls serial defibrillation. The modification consists in applying to the ventricles, through padded electrodes, a series of brief and weaker alternating current shocks. Each shock lasts less than one second and has a strength of approximately 1 ampere; one or two seconds elapse between the shocks. As a rule, from three to seven shocks suffice. The effects are that each successive alternating current shock tends to merge smaller fibrillating areas into larger ones, until a convulsive state is redeveloped. A final shock stops the fibrillation and initiates coordinated beating by natural pacemakers. It is their impression that the deeper myocardium and septum are thus included in fibrillating circuits and, in consequence, these larger circuits are interrupted without the actual passage of currents through the deeper layers and septum. The likelihood of inducing auricular fibrillation is reduced. Since September 1939, out of 328 attempts the author and Wegria have had 327 revivals and they have succeeded forty-one times in one dog. The author suggests that studies be made on larger animals to ascertain whether weaker cur-

rents might not suffice if the method of serial defibrillation were used. The difficulties of meeting the conditions necessary for reviving human fibrillating hearts are analyzed and the conclusion is reached that, although such an achievement is not impossible, remarkable results in the present state of knowledge cannot be anticipated until further methodical research suggests a way of rendering the ventricles less sensitive or refractory to fibrillating agents.

Rheumatic Heart Disease.—Clawson states that if tuberculous pericarditis is excluded, heart failure caused by an adherent pericardium appears in most cases to be the result of rheumatic infection. The condition is seldom seen except in association with rheumatic valvular involvement. From 1910 to 1937, 27,957 necropsies were performed at the University of Minnesota, and 4,254 of these revealed noncongenital cardiac disease (15.2 per cent). In 1,598 (37.6 per cent) of these the disease was infectious in origin (rheumatic, bacterial, syphilitic, toxic myocarditis). There were 796 cases of rheumatic heart disease, comprising about 50 per cent of all cases of infectious heart disease and 18.7 per cent of the cases of noncongenital heart disease. He distinguishes four types of rheumatic heart disease: acute rheumatic endocarditis, recurrent rheumatic endocarditis, valvular deformities and adherent pericardium. The respective incidence of these four types was 12.3, 9.5, 73.5 and 4.52 per cent. Death from acute and recurrent rheumatic endocarditis occurred in the early decades, from incompletely or completely healed valvular deformities in the middle decades, and from the calcific, nodular, aortic valve deformity in the later decades. Death solely as a result of adherent pericardium is rare. The sex incidence was males 27 per thousand and females 31 per thousand. Female patients died earlier than the male patients, probably because in them the mitral valve is most commonly involved. The nature of the inflammatory reaction within the valve was similar to that of frank streptococcal subacute bacterial endocarditis. The valves of the left side of the heart were involved in 99.8 per cent of the patients. There was right-sided involvement in 5.6 per cent, but this was accompanied by a lesion of one or both valves of the left side. The aortic and mitral valves were involved with equal frequency in male subjects. The predilection for the mitral valve in female patients is not understood, but it helps to explain why calcified nodular aortic deformity is common in old men. Vegetations begin on the side of the valve where the spongiosa layer is located, suggesting that the infection may be embolic in origin. However, in some cases small vessels can be seen leading from surface indentations, indicating that infection may occur directly from the blood stream. Auricular endocardial involvement was almost as common in acute rheumatic endocarditis as in bacterial endocarditis. Hypertrophy was present in most of the cases. It was most marked with aortic involvement and less pronounced when only mitral lesions were present. Hypertrophy was more marked among male patients apparently because aortic lesions are more common among them. Proliferative inflammation of a nodular (Aschoff nodules) or diffuse type was common. The stigmas of rheumatic inflammation were practically as common in the valve and myocardium among calcified nodular aortic valve deformities as in mitral valve deformities. All nonsyphilitic aortic valvular deformities which lead to cardiac failure seem to be of rheumatic origin. Tricuspid and pulmonic lesions, especially healed deformities, rarely occur without associated aortic or mitral lesions.

American Journal of Pathology, Boston

16:525-708 (Sept.) 1940

Studies of Collagen: I. Production of Collagen in Vitro Under Variable Experimental Conditions. G. Hass and F. McDonald, Boston.—p. 525.

Id.: II. Methods and Results of Implantation of Collagen-Forming Cultures in Granulation Tissue. G. Hass, Boston.—p. 549.

Dermatomyositis: Study of Five Cases. T. D. Kinney and Mary M. Maher, New Haven, Conn.—p. 561.

Eosinophilic Granuloma of Bone: Report of Case. L. Lichtenstein and H. L. Jaffe, New York.—p. 595.

Comparative Experimental Studies of 200 Kilovolt and 1,000 Kilovolt Roentgen Rays: I. Biologic Effects on Epiphysis of Albino Rat. E. A. Gall, J. R. Lingley and J. A. Hicken, Boston.—p. 605.

Familial Occurrence of Renal Carcinoma in Rhesus Monkeys (*Macaca Mulatta*). H. L. Ratcliffe, Philadelphia.—p. 619.

Teratoma of Ovary, with Segment of Vertebral Column and Remnants of Notochordal Tissue: Report of Case. J. L. Riopelle, Montreal.—p. 625.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

44:485-644 (Oct.) 1940

- Roentgenology of Pancreatic Disease: Caldwell Lecture, 1939. J. T. Case, Chicago.—p. 485.
- Recent Advances in Roentgen Examination of Neck: Body Section Roentgenography (Planigraphy) of Larynx. B. R. Young, Philadelphia.—p. 519.
- Value of Proper Interpretation of Lipiodol Bronchograms in Thoracic Surgery, with Note on Distribution of Bronchiectasis. D. W. Myers and B. Blades, St. Louis.—p. 530.
- Roentgenologic Study of Cystine Urinary Calculi. H. R. Morrison, Boston.—p. 537.
- Vertebral Column in Acromegaly. W. Chester, Mamaroneck, N. Y., and E. M. Chester, New York.—p. 552.
- Localization of Intra-Ocular Foreign Bodies with Contact Lens. R. L. Pfeiffer, New York.—p. 558.
- Course of Besnier-Boeck's Disease of Lungs in Serial Roentgenograms. E. Meisels, Lwów, Poland.—p. 564.
- Roentgen Ray in Obstetric Diagnosis. S. G. Schenck, Brooklyn.—p. 568.
- Squamous Cell Epithelioma of Cervix Uteri with Bone Metastasis: Report of Two Cases. Elma Barany and A. M. Sala, New York.—p. 579.
- Latest Results in Supervoltage Roentgen Therapy: Comparative Statistical Analysis in Selected Groups. T. Leucutia, Detroit.—p. 586.
- *Roentgen Therapy for Inflammatory Conditions: Further Considerations. A. U. Desjardins, Rochester, Minn.—p. 594.
- Comparison of Skin Reactions Produced by 200 and 1,000 Kilovolt Radiations. R. S. Stone and J. M. Robinson, San Francisco.—p. 601.
- Compact, Supervoltage, Roentgen Ray Generator Using a Pressure-Insulated Electrostatic High Voltage Source. J. G. Trump, R. J. Van de Graaff and R. W. Cloud, Cambridge, Mass.—p. 610.
- Physical Characteristics of Supervoltage Roentgen Rays. J. G. Trump and R. W. Cloud, Cambridge, Mass.—p. 615.

Roentgen Therapy for Inflammatory Conditions.—

According to Desjardins, when acute inflammatory processes, such as furuncles, carbuncles, abscess, erysipelas, parotitis, sinusitis, otitis media, pneumonia (especially delayed resolution in lobar pneumonia), are exposed early enough to a small dose of roentgen rays, rapid diminution of pain and resolution of the inflammation without suppuration follows in a large proportion. If the affected area is exposed after suppuration has developed, pain is relieved more slowly and suppuration is accelerated. When the inflammatory lesion is treated after suppuration has advanced, little or no change in the course of the process is perceived. The rate at which these alterations occur after irradiation corresponds closely to the rate at which lymphocytes, polymorphonuclear leukocytes and eosinophils are known to be affected after irradiation of normal animals. This agrees with the rate at which similar cells of human beings are influenced by irradiation. The influence, varying within certain limits with the dose of rays, consists in the destruction of a proportion of the leukocytes. Since the main effects of irradiation are exerted on cells, the sensitiveness of cells to irradiation is known to be specific for each type of cell and since the leukocytes are the only cells whose radiation sensitivity corresponds to that of acute inflammation it is concluded that the major effect of irradiating such lesions is the destruction of a proportion of the leukocytes infiltrating the inflamed tissues, of those circulating in the blood stream through and around these tissues and of the liberation of the contents of the destroyed leukocytes (antibodies, ferments and so on) into these tissues and into the blood stream. As for chronic inflammations amenable to irradiation, such as many cutaneous diseases, tuberculous adenitis, peritonitis, synovitis, keratitis and iritis, actinomycosis and many others, the pathologic circumstances differ in that leukocytic infiltration is less prominent, but the pronounced feature is proliferation of connective tissue. Connective tissue cells have such a low grade of sensitivity to radiation that they must be classed among the resistant cells. Therefore in chronic inflammatory lesions there is one factor, proliferation of connective tissue, which tends to diminish or retard the action of the rays. This is exactly what is observed in practice. The earlier chronic inflammations are treated, the better they respond. Too often, during the early stage of acute inflammations amenable to roentgen irradiation, the treatment is withheld until the inflammation has progressed beyond hope or until the best results of irradiation can no longer be expected. This situation will no doubt be corrected when more internists and surgeons become acquainted with and convinced of the value of roentgen therapy. A suitable dose of roentgen rays given in time may save some lives and in acute inflammatory processes a small or moderate dose given early will often make other treatment unnecessary.

Annals of Surgery, Philadelphia

112:801-976 (Nov.) 1940

- Personal Experiences in Vascular Surgery: Statistical Synopsis. R. Matas, New Orleans.—p. 802.
- *Clinical and Experimental Observations on Arteriovenous Fistulas. E. Holman, San Francisco.—p. 840.
- *Surgical Treatment of Aneurysm of Abdominal Aorta: Review of Literature and Report of Two Cases, One Apparently Successful. I. A. Bigger, Richmond, Va.—p. 879.
- Aneurysm of Abdominal Aorta: Treatment by Ligation. 'D. C. Elkin, Atlanta, Ga.—p. 895.
- Aneurysm of Abdominal Aorta at Its Bifurcation into Common Iliac Arteries. R. Matas, New Orleans.—p. 909.
- Experimental Studies on Gradual Occlusion of Large Arteries. H. E. Pearce, Rochester, N. Y.—p. 923.
- Prevention of Ischemic Gangrene Following Surgical Operations on Major Peripheral Arteries by Chemical Section of Cervicodorsal and Lumbar Sympathetics. M. Gage and A. Ochsner, New Orleans.—p. 938.
- Circulatory Disturbances Produced by Extensive Angiomas of Lower Extremities Associated with Varicose Veins. W. E. Lee and N. E. Freeman, Philadelphia.—p. 960.
- Heparin in Prevention of Peritoneal Adhesions: Report of Progress. E. P. Lehman and F. Boys, Charlottesville, Va.—p. 969.
- Duraluminum Enterotome for Devine Colostomy. M. Gage, New Orleans.—p. 975.

Arteriovenous Fistulas.—Holman states that since 1923, when Lewis and Drury presented observations on arteriovenous fistulas, 20 instances of this condition have been studied in man before and after their elimination, and numerous experimental animals have been observed before and after comparable fistulas were established between the larger vessels and permitted to remain for as long as seven years. Observations diametrically opposite to those of Lewis and Drury were made in some of the cases. Holman emphasizes the following points: 1. Complete cardiac decompensation with peripheral edema, ascites, hydrothorax and extreme cardiac dilatation may be corrected with a return of the heart to its normal size by eliminating a peripheral fistula. This dilatation involves not only the heart but the great vessels at its base. 2. Early evidence of the malignant influence of a fistula on the circulation—even before dilatation of the heart is detectable—is the behavior of the blood pressure and pulse following closure of the fistula by digital pressure. An increase in blood pressure and a fall in pulse rate indicate that the fistula is large and is one which is not likely to close spontaneously but is almost certain to produce increasing deleterious effects on the circulation. In 1 case, failure to heed this evidence in 1933 when the heart was normal and again in 1936 when the heart was beginning to dilate led to cardiac failure with marked dilatation in 1939. 3. This increase in blood pressure and fall in pulse rate constitute the first evidence that the circulatory bed is beginning to dilate, even though such dilatation may not yet be detectable by the usual means. 4. The extent of this increase and fall depends on the duration of the fistula and is commensurate with the extent of the dilatation of the heart and vessels proximal to the fistula being least in fistulas of short duration and greatest in those of long duration. 5. A temporary but great increase in blood pressure and fall in pulse rate may occur immediately following the operative elimination of a fistula, provided the operation is performed as a physiologic experiment without loss of blood. Despite operations for from four to six hours in 5 cases the blood pressure at the end of the operation was higher and the pulse slower than at the beginning, because of an autotransfusion from circulating blood which had increased in volume during the presence of the fistula. 6. This temporary increase and fall on closing a fistula are dependent on an increase in total blood volume, which is an inevitable accompaniment of a fistula of large size and long duration. 7. The increased blood volume is reduced immediately following operative removal of a fistula by a reduction in the plasma and a concentration of the erythrocytes and hemoglobin. 8. The increased blood volume may result in a transient overdistention of an already dilated heart following operative closure of a fistula, owing to a redistribution of the circulating blood, the volume of blood formerly diverted through the fistula into the capacious venous system now filling the central arterial bed. 9. Eight peripheral fistulas were eliminated by excision or ligation of segments of the main vessel to a limb

without any evident effect on the viability of the tissues beyond the ligature. In 1 case the common, deep and superficial femoral arteries were all ligated without nutritional impairment or function of the leg. This is explainable on the basis of the stimulus to collateral circulation that is provided by the area of diminished peripheral resistance at the site of the fistula, which attracts blood to it through all available channels. 10. When quadruple ligation of the vessels proximal and distal to the fistula is indicated, it would be desirable to ligate and divide the artery proximal to the fistula rather than to ligate it in continuity. In 1 case the fistula was reactivated by the ligature cutting through the arterial wall and reestablishing the lumen of the artery.

Surgery for Aneurysm of Abdominal Aorta.—According to Bigger, from 1817, when Sir Astley Cooper first ligated the abdominal aorta, to 1920 none of the 18 patients in whom the aorta was occluded for abdominal aneurysm survived to leave the hospital. Since 1920, 7 of 12 similar patients have been discharged from the hospital as improved and 1 other lived four and one half months but did not leave the hospital. While it is not certain that any of these patients have been cured, the results demonstrate that occlusion of the aorta is not necessarily fatal. The 2 of the 12 cases in which operation was performed by the author are reported. The first patient was a poor surgical risk in whom left-sided heart failure with pulmonary edema developed. He died following occlusion of the aorta proximal to the aneurysm. The other patient was a young man with a ruptured traumatic (gunshot) aneurysm. He had a preliminary occlusion of the aorta proximal to the aneurysm and one month later a restorative endo-aneurysmorrhaphy. One year later he appeared to be well, there was no evidence of aneurysm and the lumen of the aorta was obviously patent. The author realizes that traumatic and spontaneous aneurysms are widely different and that the treatment used for one may not be applicable for the other. For example, it is unlikely that a spontaneous aortic aneurysm would be suitable for reconstructive endo-aneurysmorrhaphy, but it seems likely that a few spontaneous aneurysms would be suitable for obliterative endo-aneurysmorrhaphy. Such procedures probably should not be attempted unless the aneurysm arises distal to the renal arteries and, almost certainly, not when the aorta is diffusely calcified. Proximal occlusion of the aorta should be a preliminary operation. This brings about shrinkage of the sac so that at the second operation the aorta or the common iliac arteries may be ligated immediately distal to the aneurysm. If the iliac arteries are permanently occluded the ligatures are to be placed on the common iliacs, and the internal iliacs (hypogastrics) should be carefully protected because of their importance as collateral channels. All possible vessels communicating with the sac should be ligated before the sac is opened. Aneurysms of the proximal portion of the abdominal aorta with such essential arteries as the celiac, superior mesenteric or both renals arising from the sac probably should not be treated surgically, while proximal ligation may be justified in aneurysms arising above the renal arteries but without any of the essential arteries originating from the sac. The author states that some of the problems of the surgical treatment of aneurysms of the abdominal aorta may be solved by carefully controlled animal experiments and others only by observations on patients with aortic aneurysms, especially those subjected to operation, and therefore careful reports of such cases are necessary. In his apparently recovered patient fascia was used to occlude the aorta at the first operation. The heavy silk ligature was left around the aorta to occlude it during the aneurysmorrhaphy in case the fascia no longer produced subtotal occlusion. The iliac arteries were exposed and heavy ligatures (tapes would have been better) passed around them for the control of retrograde bleeding when the sac was opened. In spite of these precautions there was considerable pressure in the aorta, presumably from the lumbar and middle sacral arteries which entered the aorta below the occlusion. The author is of the opinion that the strip of fascia has now completely disappeared and that the lumen of the aorta is fully restored.

Archives of Dermatology and Syphilology, Chicago

42:755-992 (Nov.) 1940

- Lichen Sclerosus et Atrophicus. H. Montgomery and W. R. Hill, Rochester, Minn.—p. 755.
Personality Factor in Psychoneurogenous Reactions of Skin. J. H. Stokes, Philadelphia.—p. 780.
*Parenteral Use of Hypertonic Dextrose for Relief of Pruritus and Serum Sickness. O. M. Stout and R. J. Kositchek, Los Angeles.—p. 802.
Sensitization to Arsenical Compounds: Sensitization to Pentavalent Arsenical Following Use of Trivalent Arsenical. A. G. Franks and S. Fisher, New York.—p. 808.
"Bubonulus" in Lymphogranuloma Venereum. R. Brandt, Augusta, Ga.—p. 811.
Arsphenamine Encephalopathy: Report of Unusual Clinical and Histologic Observations. N. A. Levy, Chicago.—p. 814.
Epithelioma Adenoides Cysticum, Tricho-Epithelioma and Basal Cell Cancer: Relation Between These Diseases as Shown by Histologic Studies of Multiple Benign Cystic Epithelioma. H. L. Traenkle, Buffalo.—p. 822.
Staphylococci Impetigo Contagiosa. S. Epstein, Marshfield, Wis.—p. 840.
Pseudo-Epitheliomatous Hyperplasia. L. H. Winer, Minneapolis.—p. 856.
Mobilization of Bismuth Produced by Ammonium Chloride. E. F. Corson, Philadelphia; H. B. Decker, Camden, N. J., and T. L. Williams, Philadelphia.—p. 868.
Transverse Furrows of Nails. Z. T. Wirtschafter and S. Littman, Cleveland.—p. 874.
Human Infection with Ecthyma Contagiosum, a Virus Disorder of Sheep: Report of Two Cases. R. Nomland, Iowa City.—p. 878.
Epidermolysis Bullosa: Clinical and Bacteriologic Study: Report of Four Cases. A. B. Cannon, M. Sanders and J. L. Rankin Jr., New York.—p. 884.
Experimental and Clinical Observations with Histaminase. A. F. Knoll and L. G. Beinbauer, Pittsburgh.—p. 896.
Effects of Nearsphenamine and Mapharsen on Formed Elements of Blood: Granulocytopenia Following Nearsphenamine Therapy in Patient Who Subsequently Received Mapharsen Without Untoward Reaction. N. N. Epstein and E. H. Falconer, San Francisco.—p. 909.
Mapharsen in Treatment of Forty Patients Following Arsphenamine Dermatitis. A. G. Schoch, L. J. Alexander and W. E. Long, Dallas, Texas.—p. 919.
*Herpes Progenitalis as a Venereal Contagion. H. Sharlit, New York.—p. 933.

Hypertonic Dextrose for Pruritus and Serum Sickness.—Stout and Kositchek observed the therapeutic effect of hypertonic solution of dextrose on patients with serum sickness and certain types of pruritus. A 5 per cent solution of dextrose by hypodermoclysis relieved the itching of a patient with exfoliative dermatitis of unknown cause. Thereafter the effects of the solution on patients with other pruritic diseases were determined. The results have been sufficiently consistent and have been sufficiently controlled to represent reliable material. In some of the cases the response of objective signs (urticaria) have paralleled the response of the subjective manifestations. The authors have not been able to establish the theoretical basis for the results. At first a 5 per cent solution of dextrose was used subcutaneously; later it was found that the intravenous route was more efficacious. The usual procedure was to administer 50 cc. of a 50 per cent solution of dextrose and to repeat this, when indicated, or to administer larger quantities of 5 or 10 per cent solutions. In several instances the effects were so instantaneous as to suggest a psychic factor. This factor was ruled out in that isotonic saline solution had no effect in 15 control cases. Of 58 patients who presented pruritus as a prominent symptom 43 were satisfactorily relieved and 15 experienced no relief. Of the 43 who responded satisfactorily, 10 had serum sickness, 7 pityriasis rosea with severe pruritus, 4 pruritus ani, 3 pruritus vulvae, 3 generalized urticaria, 3 dermatitis medicamentosa, 3 generalized exfoliative dermatitis, 2 generalized seborrheic dermatitis and 1 each generalized lichen planus, pruritic papular secondary syphilis, keratoderma climactericum, neoplastic obstructive jaundice, lymphoblastoma cutis, vegetative pemphigus, dermatitis herpetiformis and generalized erythema multiforme. Of the 15 who failed to respond, 5 had infectious eczematoid dermatitis, 4 poison oak dermatitis, 5 senile pruritus, 1 pruritus vulvae, 1 generalized seborrheic dermatitis and 1 atopic eczema with asthma. In the controls after 50 cc. of isotonic saline solution was given intravenously neither objective nor subjective relief was obtained. From one half to several hours after the saline solution was given dextrose was administered with immediate results. In 4 cases in which itching had been a prolonged symptom and in which periodic injections of dextrose controlled the pruritus, substitution of saline solution without the patient's knowledge demonstrated that the dex-

trose produced relief and the saline solution did not. The most noteworthy results were obtained by the 10 patients with serum sickness. The results were immediate, consistent and complete; not only was the pruritus relieved but the accompanying pains in the joints, urticaria and fever. Three of them had previously failed to respond to intensive treatment with epinephrine and calcium gluconate.

Herpes Progenitalis as a Venereal Contagion.—Sharlit believes that the evidence he presents unequivocally establishes herpes progenitalis as a venereal contagion. He presents the histories of 2 patients whose reliability of the pertinent facts argues acceptance of the venereal source of herpes progenitalis and suggests that this clinical entity be included in the group of venereal diseases. The histories are as follows: In February 1928 a white man immediately after sexual intercourse noticed a papule on his penis. That night lightning pains developed in the right groin, and the next morning, when he called on the author, he observed a slight swelling in the right inguinal region. Examination showed a solitary papule on the dorsal surface of the shaft of the penis which was capped by a ruptured vesicle. The skin about the base of the papule was deeply red; a burning pain was present in the lesion and pains radiated to the right groin. The right inguinal nodes were enlarged and tender. The patient had never had a genital "sore" of any kind before. In the preceding twelve months the patient, with one exception, had had sexual relations with only one woman. The exception occurred just six days before his appearance at the author's office. A dark field examination of the lesion showed no spirochetes. A Wassermann test of the woman "of a week ago" was negative. She refused to be examined. A provisional diagnosis of genital herpes was made. Five days after the patient's first visit he returned and brought with him the woman of his constant attention. The night before she had a burning pain in the right vulvar region and on examination an eruption was revealed; tiny vesicles on a deeply congested background on the right labium majus. The condition was typical herpes simplex, the first and only herpes progenitalis that the author has seen in a woman. This woman had never had a genital lesion. The woman's history extended for but one year from her first visit, during which time she had one recurrence of genital herpes in approximately the same region. The man's history has now been available for twelve years. During this time he has had at least a dozen recurrences of herpes progenitalis, on the shaft and on the corona. He has never again had a solitary papule covered by a vesicle but always grouped vesicles. The last two attacks, however, have been on the right buttock. The author believes that his cases are evidences of contagious inoculation, albeit apparently the first. He sees in them missing links in the chain of a rationalized epidemiology. He hopes that careful and detailed studies of the histories of cases of herpes progenitalis will be made to the end that the epidemiology of their infectiousness may be convincingly clarified. The pertinent facts of 2 cases from the private records of Charles Rein of New York are given: A woman, receiving treatment for frequently recurring genital herpes, married during the period of treatment. Nine months after marriage an initial attack of penile herpes occurred in the husband and was followed by recurrences. The rarity of genital herpes minimizes coincidence as explanatory of these 2 cases in conubium. The fact that the husband had approximately nine months of exposure before becoming infected has immunologic significance.

Archives of Pathology, Chicago

30:993-1158 (Nov.) 1940

- Giant Cell Tumor of Bone: Its Pathologic Appearance, Grading, Supposed Variants and Treatment. H. L. Jaffe, L. Lichtenstein and R. B. Portis, New York.—p. 993.
Factors Governing Solubility of Human Gallstones in Dog's Bile. H. G. Aronson, Chicago.—p. 1032.
Wave Mechanics in Striated Muscle: XVI. Effects of Experimental Variations in Temperature and of Microcapillarity on Cross Striations in Muscle. E. J. Carey, Milwaukee.—p. 1041.
Pigmented Cells of Pia and of Meningeal Tumors. A. E. Taft, Philadelphia.—p. 1073.
Role of Fixed Tissue Phagocytes in Lipid Metabolism. E. F. Hirsch and S. Weinhouse, Chicago.—p. 1079.
Lysozyme and Its Relation to Antibacterial Properties of Various Tissues and Secretions. R. Thompson, New York.—p. 1096.

Archives of Surgery, Chicago

41:1043-1304 (Nov.) 1940

- Diseases of Esophagus: Esophagoscopy Considerations. L. H. Clerf, Philadelphia.—p. 1043.
*Congenital Atresia of Esophagus: Study of Thirty-Two Cases. T. H. Lanman, Boston.—p. 1060.
Roentgen Demonstration of Esophageal Varices: Its Clinical Importance. R. Schatzki, Boston.—p. 1084.
*Bleeding Esophageal Varices: Evaluation of Methods Directed Toward Their Control, Especially by Direct Injection of Sclerosing Solution. W. Walters, H. J. Moersch and D. A. McKinnon, Rochester, Minn.—p. 1101.
Esophageal Diverticula. F. H. Lahey, Boston.—p. 1118.
Conservative Treatment of Achalasia. E. B. Freeman, Baltimore.—p. 1141.
Surgical Considerations of Achalasia: Review of Literature and Report of Three Cases. A. Ochsner and M. DeBakey, New Orleans.—p. 1146.
Surgical Treatment of Carcinoma of Esophagus. J. H. Garlock, New York.—p. 1184.
Malignant Tumors of Hernial Sacs. L. M. Zimmerman and H. Laufman, Chicago.—p. 1215.
Congenital Absence of Sacrum. I. M. Zelig, Iowa City.—p. 1220.
Femoral Hernias: Study of 238 Hernias and 226 Repairs. H. J. Shelley, Fort Worth, Texas.—p. 1229.
Parenteral Administration of Water-Soluble Compound with Vitamin K Activity: 4-Amino-2-Methyl-1-Naphthol Hydrochloride. E. R. Anderson, J. E. Karabin, H. Udesky and L. Seed, Chicago.—p. 1244.
Role of Intraluminal Obstruction in Pathogenesis of Acute Appendicitis. H. Koster and A. Shapiro, Brooklyn.—p. 1251.
Fibrosarcoma of Soft Tissue Producing Regional Concentric Bone Absorption. O. C. Julian, Chicago.—p. 1257.
Review of Urologic Surgery. A. J. Scholl, Los Angeles; F. Hinman, San Francisco; A. von Lichtenberg, Budapest, Hungary; A. B. Hepler, Seattle; R. Gutierrez, New York; G. J. Thompson, J. T. Priestley, Rochester, Minn.; E. Wildbolz, Bern, Switzerland, and V. J. O'Connor, Chicago.—p. 1272.

Congenital Atresia of Esophagus.—Lanman presents an analysis of 32 cases of congenital atresia of the esophagus observed at the Children's Hospital during the last eleven years. Thirty of the patients were submitted to operation. A complete necropsy was performed on 2. The observations on the 30 operative cases were supplemented by complete post-mortem examination of 22. Despite the fatal outcome in all of the 30 operative cases, the author believes that considerable progress along rational lines is being made and that successful operative treatment is only a question of time. For a successful outcome it is essential that the condition be recognized during the first few hours of life. Any infant presenting characteristic signs or symptoms of esophageal atresia should have a catheter passed down the esophagus and roentgenograms performed without opaque medium. Immediate operation is imperative if obstruction is present. The author states that anterior gastrostomy is futile unless the lower segment does not communicate with the trachea. Regardless of what procedure other than a direct anastomosis is used for the lower segment, the upper segment must be treated so that aspiration of the overflow of secretions from this blind pouch is prevented. Constant suction is dangerous. Early exteriorization of this upper segment has been advocated and used at the Children's Hospital without success, though, the author states, it is possible that it would have been successful in three of the cases had a posterior esophagostomy not been added to the closure of the fistula at the first operation. Exteriorization of the upper segment commits the patient, if he survives, to a permanent exterior esophagus. Treatment of the lower segment, except in cases with a blind end to the upper and lower segments of the esophagus and in those in which the upper segment communicates with the trachea and the lower segment is blind, must include measures which will prevent contents from the lower segment from entering the trachea. Some of the procedures suggested do not do this. It is the author's belief that no method of attack that does not have as its first step direct closure of the fistula between the lower segment and the trachea has any reasonable chance of success, particularly as regards a primary anastomosis. Direct exposure of the fistula by the extrapleural approach, he believes, should be undertaken. The extrapleural approach seems to be safer than the transpleural. If direct anastomosis is possible it should be done, and if successful and no complication develops the problem is solved, barring possible esophageal stenosis later. If direct anastomosis appears impossible or inadvisable the tracheo-esophageal fistula should be closed and nothing further done at this time. Subsequent procedures as soon as conditions permit are exteriorization of the upper esophageal segment and

anterior gastrostomy. If the patient survives, construction of an exterior connection between the upper esophagostomy and the anterior gastrostomy can then be postponed until a suitable age. An exterior esophagus as a palliative procedure for an elderly patient with cancer is justifiable and endurable, but one dreads to commit an infant to such an existence.

Bleeding Esophageal Varices.—Walters and his associates conclude that esophageal varices develop as a result of obstruction of the portal and splenic veins and that bleeding occurs because of their superficial position in relation to the esophageal mucosa. Banti's disease and splenic anemia are frequently associated with esophageal varices. They cannot be regarded as distinct clinical entities, as they may result from obstruction of the portal or splenic vein. The surgical treatment of splenic anemia has been directed toward removal of the enlarged spleen. Although it has been followed by good results in a large series of cases, the operation does not prevent recurrence of bleeding from the esophageal varices in more than 38 per cent of the cases even when combined with ligation of the coronary vein or with omentopexy. According to Mayo, in about 10 per cent of the cases in which recovery has taken place after splenectomy, death has occurred some time in the next ten years of hemorrhage from the stomach, probably from ruptured varices in the lower end of the esophagus. Although ligation of the coronary vein in the gastrohepatic omentum will serve to interrupt considerable flow of blood through it, the procedure has been used alone in too few cases of splenic anemia to justify any conclusion of its merits in reducing the incidence of hemorrhages from esophageal varices. The recent successful obliteration of esophageal varices by injecting sclerosing solutions into them through the esophagoscope, and their use of the method in 6 cases, lead the authors to believe that the procedure is worthy of trial. Sufficient time has not elapsed to determine whether further bleeding will occur making repetition of the method necessary. The authors believe that the procedure offers a method of controlling bleeding that has not responded to any other form of therapy and thus may be successful in prolonging the life of the patient.

Arkansas Medical Society Journal, Fort Smith

37:113-134 (Nov.) 1940

Medical Education in the United States 1934-1939. S. P. Cromer, Little Rock.—p. 113.

Diagnosis and Treatment of Ectopic Pregnancy. B. L. Moore, El Dorado.—p. 116.

Bulletin New York Academy of Medicine, New York

16:657-720 (Nov.) 1940

Pathologic Aspects of Rheumatic Fever. C. E. de la Chapelle, New York.—p. 659.

Treatment of Mental Disease in France at the End of the Eighteenth Century. C. P. Oberndorf, New York.—p. 670.

Review of Maternity Statistics of New York City for the Year 1939. T. J. Duffield, New York.—p. 679.

Connecticut State Medical Journal, Hartford

4:637-706 (Nov.) 1940

Beginnings of Medical Practice in New Haven Colony. H. Thoms, New Haven.—p. 639.

Emergency Treatment of Fractures. C. R. Murray, New York.—p. 645.

*Results of Four Types of Therapy in 165 Cases of Pneumonia. P. J. Steincrohn, Hartford.—p. 653.

Fundamental Principles of Treatment of Gonococcal Infections of Women. R. M. Lewis, New Haven.—p. 662.

Problems Relating to Diphtheria Toxoid Immunization. M. M. Hillman, New Haven.—p. 664.

Treatment of Compound Fractures. D. C. Patterson, Bridgeport.—p. 666.

Tumors of Lateral Aberrant Thyroid Tissue: Report of Two Cases. W. A. Geer, Bridgeport.—p. 670.

Four Types of Therapy for Pneumonia.—Steincrohn discusses four types of treatment used for 165 pneumonia patients treated in his medical service at the Municipal Hospital during February, March and April of the years 1934 to 1939. The treatments were routine, concentrated dextrose intravenously, serum and sulfapyridine. The mortality for 1934 through 1938 was 35 per cent for all ages. Among patients less than 60 years of age the rate was 20.4 per cent, rising to 60.3 per cent in those more than 60. The mortality in patients with coex-

isting disease was 42.1 per cent as against 17.6 per cent free from complications. Although the mortality rate for the dextrose treated patients was higher (38.4 per cent) than those routinely treated (32.4 per cent) intravenous dextrose therapy has its place in the treatment of individual indications. The average age of the 46 patients who died during the 1934 to 1938 period was 49.3 years and of the 29 given sulfapyridine in 1939 it was 52.3 years. In view of the fact that almost 50 per cent of the patients in the latter group were more than 60 years of age, the sulfapyridine mortality of 8.3 per cent (excluding death within twenty-four hours of admission) is startling as compared with the revised mortality of 30.2 per cent for the patients receiving routine dextrose and serum treatment. In his small series the author observed a definite leukocytic response to sulfapyridine. In the majority of patients who recovered there was a relative leukopenia in from twenty-four to forty-eight hours. The author felt that the absence of a leukopenic response made for a poor prognosis. A marked leukopenia with a normal differential count is no contraindication to the further administration of sulfapyridine. A high concentration of sulfapyridine in the blood does not necessarily indicate a good prognosis. The average number of days of illness before admission in the entire series was practically the same. Patients treated with sulfapyridine were free from fever in an average of 1.6 days, and the 1934 to 1938 group in 9.4 days. The mortality rate of 17.6 per cent among the serum treated patients bears out the accepted experience that serum treatment cuts routine treatment mortality in half. The comparative results of the four treatments demonstrates that no patient with pneumonia should be deprived of the unquestionable aid of sulfapyridine or serum therapy.

Delaware State Medical Journal, Wilmington

12:213-230 (Oct.) 1940

Complicated Labor, with Special Reference to Use of Forceps. C. H. Davis, Wilmington.—p. 213.

Endocrinology, Los Angeles

27:707-842 (Nov.) 1940. Partial Index

Study of Metabolism of Crystalline Progesterone. Eleanor H. Venning and J. S. L. Browne, Montreal.—p. 707.

Effect of Estrogens on Pregnanediol Output During the Menstrual Cycle. C. J. Pattee, Eleanor H. Venning and J. S. L. Browne, Montreal.—p. 721.

Alteration of Urinary Excretion of Androgens by Estrogenic Therapy. E. C. Hamblen, Durham, N. C.; C. J. Pattee, Montreal, and W. K. Cuyler.—p. 734.

*Oral Administration of Diethylstilbestrol Dipropionate. B. B. Weinstein, J. C. Weed, F. R. Lock and C. G. Collins, New Orleans.—p. 739.

Castration in the Male: Notes on Hypothalamicopituitary-Gonadal System. R. C. Moehlig, Detroit.—p. 743.

Endocrine Dyscrasia of Acne Vulgaris in Women. C. H. Lawrence and N. T. Werthessen, Boston.—p. 755.

Blood Sugar Studies in Case of Adiposogenital Dystrophy Showing Chronic Hypoglycemia. J. F. Hart, New York.—p. 759.

*Treatment of Obesity Due to Dietary Indiscretion (Overeating) with Benzedrine Sulfate. J. S. Ersner, Philadelphia.—p. 776.

Does Testosterone Propionate Inhibit Ovulation? H. O. Burdick, Alfred, N. Y.—p. 825.

Oral Administration of Diethylstilbestrol Dipropionate.

—Weinstein and his associates gave diethylstilbestrol dipropionate orally to 51 women complaining of physiologic menopausal symptoms, to 35 having menopausal symptoms that were initiated by roentgen or surgical treatment, to 6 young women suffering from hypo-estrogen symptoms and to 8 women with atrophic genital changes. The therapeutic regimen for the first group consisted of 1 mg. of diethylstilbestrol dipropionate three times a day. After one week the patient's response to the medication was ascertained and further dosage varied with the individual's reaction. When symptoms were mild or markedly improved the daily dose was reduced to 0.3 mg., whereas the daily dose of those giving little or no response was increased to as much as 15 mg. Twenty-five of these patients were relieved of all symptoms, 16 were improved, 3 showed only slight improvement and 7 exhibited no response. The basis of the treatment of patients with artificial menopausal symptoms was that employed for the preceding group. Individualization of therapy was followed. Generally a large maintenance dose was necessary for relief of this group; 19 were completely relieved, 13 were improved, 2 were slightly improved and 1 experienced no improvement. For the 6 young women exhibit-

ing evidence of hypo-estrogenism (as manifested by menstrual irregularities, headaches, nervousness, irritability, occasional hot flushes, anxiety, depression and diminished libido) individualization of therapy was essential. As most of the complaints were of a cyclic nature, usually preceding or associated with the menstrual flow, the drug was used at that time. All 6 were improved. The atrophic changes of the genitalia in 3 of the 8 women followed artificial menopause, 4 were associated with the physiologic menopausal syndrome and 1 exhibited senile vaginitis without concomitant menopausal symptoms. Here again therapy was individualized. Keratinization of the vaginal epithelium followed the oral administration of the drug. This was observed within as short an interval as one week, and with as little as 7 mg. of the drug. Usually three weeks elapsed and 21 mg. of the drug was necessary before complete relief was obtained. All patients were completely relieved, but recurrences were frequent in from six to twelve weeks after treatment was stopped. Diethylstilbestrol dipropionate orally controls the senile vaginitis, and keratinization of the vaginal epithelium takes place, but the associated atrophic changes do not show the same degree of regression that follows the vaginal administration of biologic estrogens. The only toxic manifestations evidenced by 15 per cent of the women were nausea and vomiting. Only 1 patient was completely intolerant to the drug.

Amphetamine Sulfate for Obesity.—Ersner states that in more than 500 cases of obesity amphetamine sulfate has proved to be the "drug of choice" in obtaining excellent results. No serious complications were encountered. Only obese patients who gave a history of overeating were selected for treatment. After a physical examination the patient was put on a diet of from 1,200 and 1,500 calories daily. This diet consisted of dry cereals, skimmed milk, tea or coffee (without sugar or cream) fresh and stewed fruits, raw and cooked vegetables, one slice of bread with each meal and the choice of from 6 to 8 ounces of meat, fish, chicken, cottage cheese or two eggs daily. The patient was cautioned to limit the intake of fluid and to make certain of a daily evacuation. The patient was given the first week's medication (the smallest possible dose) and thereafter returned every week for a check-up and further medication. The drug was withdrawn at the end of every month or the loss of the first 20 pounds (9 Kg.) and subsequent 15 pounds (6.7 Kg.), and for the ensuing week some brand of vitamin B, C and G was prescribed to make up for any deficiency in the diet caused by the patient's carelessness. After each of these vitamin periods the previous week's dosage was again prescribed and then increased the following week. This permitted the final strength of the drug, one 10 mg. tablet after each meal, to be reached in about three months. The amount of weight to be lost at any one course of treatment was never to be more than one fifth or one sixth of the patient's greatest weight. If the new final weight was far from the nearest calculated normal chart weight (according to height and age), the patient was instructed to return in from four to six months, when again this procedure would be repeated. Thus no patient in the series showed any untoward effects from the loss of weight, even though as much as 60 pounds (27 Kg.) was lost by 1 patient in the course of three months. The average weight lost for the first week amounted to 5 pounds (2.3 Kg.). The average loss for a course of treatment (from three to twelve weeks) was 3½ pounds (1.4 Kg.) per week. With the exception of the vitamin week there were but few occasions when a continuous and sustained loss of weight was not obtained; 100 per cent cooperation was requested. Invariably most of the patients would voluntarily say that they were feeling much better or had much more pep. All agreed that the loss of appetite made dieting easy. With the small graduated doses of amphetamine sulfate employed, the systolic and the diastolic readings, when hypertension was present, usually dropped to normal. Whether this drop toward normal was directly due to the action of the drug or to the loss of weight is a question. Several instances of hypotension became normal during the course of treatment. Normal blood pressures were not affected or were slightly, if at all, lowered. There was but little change in the metabolic rate during the course of treatment. A marked progressive improvement in urines containing albumin, sugar and hyaline and granular casts was observed,

indicating that amphetamine sulfate produces no injurious renal effects. There was little evidence of true addiction. In most instances the medication caused a mild constipation, which was easily remedied with a mild laxative or a simple lubricant, as liquid petrolatum. The reported untoward reactions of the drug should be of much significance to the dispenser and the novice who is about to prescribe it. The patient must be educated as to the possibility of its allergic reactions and of its cumulative effects. Self medication and overdosing must be eliminated to prevent any future fatalities.

Indiana State Medical Assn. Journal, Indianapolis

33:603-644 (Nov.) 1940

- World Affairs and Medicine. K. R. Ruddell, Indianapolis.—p. 603.
Acute Nephritis. J. M. Hayman Jr., Cleveland.—p. 605.
Evolution and Revolution in Medical Practice. N. K. Forster, Hammond.—p. 609.
Roentgenologic Aspects of Pulmonary Mycotic Infection. R. C. Beeler, J. N. Collins and W. M. Lochr, Indianapolis.—p. 613.
Auriculoventricular Heart Block with Stokes-Adams Syndrome in Patient with Syphilitic Heart Disease and Diffuse Myocarditis. C. Bohnengel, New York.—p. 617.
*Relationship Between Various Types of Kidney Disease and Hypertension. W. L. Ritter, Indianapolis.—p. 620.
Ancient Pronunciation of Medical Words. M. Thebaut, Oakland, Calif.—p. 623.

Kidney Disease and Hypertension.—Ritter studied the relationship between urologic abnormalities and arterial hypertension. He analyzed data from 28 patients with such abnormalities and from 24 patients suffering from hydronephrosis or renal anomalies with or without stones or secondary infection. The patients in the first group had developmental urinary anomalies. Among them there were 4 who had elevated blood pressures, more than 140 systolic and more than 90 diastolic. These cases give an incidence of 14.2 per cent, which is not greater than that which occurs among the apparently normal population. Persons with renal anomalies are apparently not appreciably more subject to hypertension than are normal people. The patients of the second group were admitted to the Indianapolis City Hospital from five to ten years ago and were chosen because at the time of their first observation their blood pressures were normal, less than 140 systolic and 90 diastolic. Blood pressure elevations did not develop in any of these patients during the interval, although many had had recurrent urinary infections or lithiasis and colic. The author concludes that since neither renal anomalies nor hydronephrosis with or without lithiasis or infection leads to hypertension an increased incidence of pyelographic abnormalities among patients with hypertension might be better explained by the assumption that the humoral substances responsible for hypertension may also act on the kidneys and ureters to produce these distorted shadows.

Johns Hopkins Hospital Bulletin, Baltimore

67:309-376 (Nov.) 1940

- Sickling Phenomenon, with Special Reference to Differentiation of Sick Cell Anemia from Sick Cell Trait. I. J. Sherman, Baltimore.—p. 309.
Immunity in Relation to 1:2:5:6-Dibenzanthracene-Induced Sarcomas. Margaret Reed Lewis, Baltimore.—p. 325.
*Electrolyte Changes in Pulmonary Tuberculosis, with Special Reference to Adrenal Cortical Function. G. W. Thorn, R. P. Howard, Baltimore, and H. Dayman, Ray Brook, N. Y.—p. 345.
*Influence of Experimental Escherichia Coli Infections in Mice.—p. 365.
on Arm and Thorax of Man. P. H. —p. 365.

Electrolyte Changes in Pulmonary Tuberculosis.—Thorn and his associates investigated the blood serum concentration of sodium, chloride, potassium, carbon dioxide combining power and plasma volume of 104 patients with pulmonary tuberculosis in an effort to determine whether adrenal cortex insufficiency existed. Nine healthy men living in the same environment and 7 patients suffering from widespread nontuberculous pulmonary disease (silicosis) were chosen as controls. Because the menstrual cycle has a marked effect on electrolyte balance, only male patients were used for the study. All the patients were provided with an adequate intake of sodium chloride during a preliminary control period. A summary of the observations revealed a significant decrease in serum chloride concentration in patients with pulmonary tuberculosis and in patients with extensive nontuberculous pulmonary disease. The

decrease in serum chloride paralleled closely the decrease in the vital capacity of these patients. The serum bicarbonate concentration of patients with extensive pulmonary disease was increased but it did not equal in magnitude the reduction in serum chloride. There was no significant alteration in the concentration of serum sodium or potassium in either group. The hematocrit (percentage cell volume) of patients with pulmonary tuberculosis and extensive nonpulmonary disease was greater than normal. Blood volume studies and examination of the erythrocytes usually indicated an increase in their number and in their total volume. This was associated with a corresponding decrease in the volume of blood plasma. In 48 of 60 patients with pulmonary tuberculosis, a three day regimen of low sodium chloride intake with supplementary potassium did not precipitate signs or symptoms of adrenal cortex insufficiency. With the exception of a considerable decrease in serum chloride concentration the changes in serum electrolytes, body weight and blood pressure during this period were within normal limits. The urinary concentrations of sodium and chloride on the third day of the test were also within normal range. The appreciable weight loss, the higher than normal urinary concentration of sodium and chloride and the anorexia and weakness which occurred in 2 patients suggested that they may have had some degree of adrenal cortex insufficiency. Patients with pulmonary tuberculosis differed from those with Addison's disease in that they maintained a normal serum concentration of sodium and potassium, preserved a normal total blood volume and withstood a regimen of sodium chloride deprivation with supplementary potassium medication without changes in body weight, blood pressure and urinary concentration of sodium and chloride typically observed in adrenal cortex insufficiency. When acidosis or renal disease is absent the response to the Cutler, Power and Wilder sodium chloride deprivation test is of great aid in differentiating patients with pulmonary tuberculosis from those in whom the pulmonary tuberculosis is complicated by adrenal cortex or anterior pituitary deficiency.

Journal of Clinical Investigation, New York

19:795-888 (Nov.) 1940

- *Origin and Nature of Normal Human Synovial Fluid. Marian W. Ropes, Elsie C. Rossmelst and W. Bauer, Boston.—p. 795.
Excretion of Sodium Pregnanediol Glucuronide in Urine of Normal Human Pregnancy. C. Bachman, Dorothy Leekley and H. Hirschmann, Philadelphia.—p. 801.
*Effect of Large Doses of Vitamins A, B, C and D on Incidence of Upper Respiratory Infections in Group of Rheumatic Children. Ann G. Kuttner, Irvington-on-Hudson, N. Y.—p. 809.
Carbohydrate Metabolism in Addison's Disease. G. W. Thorn, G. F. Koepf, R. A. Lewis and Elizabeth F. Olsen, Baltimore.—p. 813.
Choline Esterase of Blood Cells and Plasma in Blood Dyscrasias, with Special Reference to Pernicious Anemia. Jean Captain Sabine, Rochester, N. Y.—p. 833.
Fat Metabolism in Diabetes Mellitus. W. C. Stadie, Philadelphia.—p. 843.
Basal Gastric Secretion as Clinical Test of Gastric Function, with Special Reference to Peptic Ulcer. A. L. Bloomfield, Chen Kuo Chen and L. R. French, San Francisco.—p. 863.

Origin and Nature of Normal Human Synovial Fluid.

—In an endeavor to determine whether the synovial fluid of human beings is a dialysate of plasma containing albumin, globulin and mucin, as is bovine synovial fluid, Ropes and her associates studied the synovial fluid immediately after death of 124 patients who had had no signs or symptoms of joint disease. The study indicated that bovine and human synovial fluids are essentially the same, as the distribution of nonelectrolytes and electrolytes between plasma and normal human synovial fluid were in accord with the observations in normal bovine synovial fluid. Normal human synovial fluid is a dialysate of blood plasma and contains albumin, globulin and mucin. The presence of mucin distinguishes synovial fluid and similar connective tissue fluids from other body fluids that are dialysates of plasma.

Vitamins and Respiratory Infections.—Kuttner studied the effect of adding an excess of vitamins A, C, D and B complex to an average diet of half of 108 rheumatic children from 7 to 14 years of age admitted for institutional care, who remained in the institution from December until the end of May. Children with definite histories of one or two attacks of polyarthritis or carditis without severe cardiac damage were selected. The effect of the addition of the vitamins was studied during two successive winters. Half of the 108 children received

the regular diet with the addition of vitamins, and the other half received the regular diet but were given no additional vitamins. The children in the two groups were matched as nearly as possible as to rheumatic history, age and general condition. Beginning in February 1939 and continuing through May, infections of the upper respiratory track developed in 32 children. These infections were associated with the presence of group A beta hemolytic streptococcus of a single type, type 4. Most of the children complained of sore throat and had temperatures of from 101 to 103 F. for two or three days accompanied by elevated leukocyte counts. Type 4 streptococci were isolated from throat cultures and were usually present in large numbers. Rheumatic manifestations following these respiratory infections did not develop in any of the 32 children. The average gain in weight during the five months for the boys in the two groups was the same. The average weight gain among the girls receiving vitamins was 1½ pounds (0.7 Kg.) more than among those serving as controls. During the winter of 1939-1940 two types of respiratory infections were prevalent among the children: an outbreak of 51 cases of influenza (characterized by fever, malaise and a low leukocyte count) and 24 sore throats accompanied by fever and elevated leukocyte counts. Throat cultures from the influenza cases were negative for beta hemolytic streptococci. Throat cultures from the cases of pharyngitis showed group A beta hemolytic streptococci of a single type, type 27. Of the 13 children who were not receiving vitamins and who contracted type 27 infections a rheumatic recurrence following a latent period developed in only 1. Of the 11 children who were receiving vitamins and who contracted type 27 infections, rheumatic recurrences following a latent period developed in 3. The latent periods were respectively, eighteen, twenty-two and twenty days. The administration of vitamins to these 3 children was never interrupted and therefore the rheumatic recurrence developed in spite of the administration of large amounts of vitamin C. Of the 51 children who had influenza, 26 were receiving vitamins and 25 were in the control group. In contrast to the previous year, the average gain in weight of the boys receiving vitamins was slightly greater than of the control boys and the gain in weight among the two groups of girls was the same. Children receiving institutional care usually tend to gain and therefore no definite improvement can be attributed to the vitamins. No evidence was obtained suggesting that the addition of large doses of vitamins A, B complex, C and D to an ordinary well balanced diet reduces the incidence of infections of the upper respiratory tract.

Journal Industrial Hygiene & Toxicology, Baltimore

22:303-380 (Oct.) 1940

- Control of Tuberculosis: I. Pulmonary Tuberculosis in Applicants for Employment. Ada Chree Reid, New York.—p. 303.
Physiologic Response of Animals to Some Simple Mononitroparaffins and to Certain Derivatives of These Compounds. W. Machle, E. W. Scott and J. Treon, Cincinnati.—p. 315.
How Toxic Is Arsenate of Lead? I. D. Cardiff, Yakima, Wash.—p. 333.
Chemical and Physiologic Investigation of Electric Arc Welding: I. Bare, Washed Welding Rods. G. C. Harrold, S. F. Meek and C. P. McCreight, Detroit.—p. 347.

Journal of Infectious Diseases, Chicago

67:81-176 (Sept.-Oct.) 1940

- Abrupt Increase in Resistance to Crotalus Venom. P. Kyes, L. Markin and O. J. Graham, Chicago.—p. 81.
Survival of Pneumococci in Empyemic Fluid: Effect of Sulfapyridine on Their Viability. E. Neter, Buffalo.—p. 84.
Failure of Shocking Agents to Influence Mode of Spread of Various Viruses in Central Nervous System. Margaret Holden, New York.—p. 88.
Bacteriologic Studies on Experimental Dental Caries in Rat: I. Bacterial Flora of Normal, Noncarious Teeth. R. W. Harrison, Chicago.—p. 91.
Id.: II. Changes in Tooth Surface Flora Associated with Development and Inhibition of Dental Caries. R. W. Harrison, Chicago.—p. 97.
Id.: III. Flora of Advanced Carious Lesions. R. W. Harrison, Chicago.—p. 106.
Sodium Azide as Inhibiting Substance for Gram-Negative Bacteria. M. L. Snyder and H. C. Lichstein, Ann Arbor, Mich.—p. 113.
Experimental Poliomyelitis in Animals Other Than the Monkey: II. Effects of Nonspecific Intracerebral Injections in Rabbits. J. A. Toomey and W. S. Takacs, Cleveland.—p. 116.
Hematology of Malaria (Plasmodium Brasiliense) in Panamanian Monkeys: I. Numerical Changes in Leukocytes. W. H. Taliaferro and Cessa Klüver, Chicago.—p. 121.
Id.: II. Morphology of Leukocytes and Origin of Monocytes and Macrophages. W. H. Taliaferro and Cessa Klüver, Chicago.—p. 162.

60:433-478 (Oct.) 1940

- Preventive Allergy in Infancy and Childhood. A. V. Stoesser, Minneapolis.—p. 433.
 Treatment of Common Diseases of Skin. L. A. Brunsting, Rochester, Minn.—p. 438.
 Medical Observations in India. L. J. Alger, Grand Forks, N. D.—p. 442.
 Early Diagnosis of Acute Appendicitis in the Preschool Child. M. Seham and A. J. Moss, Minneapolis.—p. 444.
 Choice of Operation for Vesical Neck Obstruction. F. E. B. Foley, St. Paul.—p. 449.
 The Physical Education Teacher as Health Counselor. T. B. Kirkpatrick, New York.—p. 451.
 *Cold Prevention Studies: Abortive Treatment with Benzdrine and with Codeine-Papaverine Mixture. A. B. Baker and D. W. Cowan, Minneapolis.—p. 453.
 Acute Exanthemas and Their Differential Diagnosis in the College Age Group (Colored Photography as Aid in Teaching Problems). L. R. Cole, Madison, Wis.—p. 456.
 *Treatment of Uncomplicated Acute Alcoholism: Preliminary Report on Effectiveness of Insulin, Glucose and Thiamine Chloride in Correcting Pathologic Physiology. G. W. Robinson Jr. and P. Shelton, Kansas City, Mo.—p. 461.

Cold Prevention Studies.—Baker and Cowan present studies on the incidence of colds among university students using amphetamine inhalers or a codeine-papaverine mixture and those employing a placebo for aborting colds at the first onset of symptoms. There were 279 students who used the amphetamine inhaler and 276 who used inhalers except that they contained no amphetamine but in appearance and odor were indistinguishable from those containing the drug. During the two years of the study the amphetamine group reported an average of 1.3 colds per person annually. This represented a reduction of 76 per cent from the average of 5.5 colds per person annually which the same students reported for the two years prior to the study. The control group reported a fall from 5.1 previous colds to 1.9 colds per person annually during the study. This represents a reduction of 63 per cent and certainly nullifies the apparent benefit given by the amphetamine inhaler. There was no difference between the two groups in number of days lost from school. The codeine-papaverine mixture was taken by 224 students and among them there was a reduction of 80 per cent in the average number of colds per person annually during the two years of the study as compared to the two previous years as compared to the reduction of 63 per cent for the control group. The results for the codeine-papaverine mixture, like those for the amphetamine inhaler, are not significantly different. An attempt to summarize the complications of the common cold which occurred during the period of the study, although the number is small, indicates that the codeine-papaverine group presented only about 50 per cent as many complications as the amphetamine group, a previously vaccinated group or the control group.

Treatment of Uncomplicated Acute Alcoholism.—For the last two and a half years Robinson and Shelton have treated their acute alcoholic patients without complicating neurosis or psychosis by correcting the metabolic disturbances by the use of insulin, intravenous dextrose, thiamine hydrochloride and a high caloric diet. One hundred and eighty-six individual patients suffering from acute alcoholism were treated by reestablishing their carbohydrate metabolism; 166 were readmitted, making a total of 352 admissions or patient procedures. Immediately after admission, 20 units of insulin is given and at the first sign of hunger liquid nourishment is provided. If the patient insists on a drink he is given one. The patient must be watched carefully and if the intensity of perspiration increases he is aroused if asleep and urged to take liquids. As an increase in perspiration is evidence of a minor insulin reaction, the patient is usually hungry and cooperative. A second dose of 20 units of insulin is given three hours after the first. This almost invariably produces hunger and the patient will take quantities of liquid food and some may take light solids. After this meal the average patient usually falls asleep and sleeps naturally for several hours. He may wake up nervous and some patients may want alcohol. Shortly after he awakens he is given 500 cc. of a 10 per cent solution of dextrose containing 10 units of insulin and 10 mg. of thiamine hydrochloride. This frequently controls all the nervous symptoms and produces complete relaxation. One or

two subsequent infusions may be given if warranted. Twenty units of insulin is given at 6 and 9 p. m. of the second hospital day, and the patient usually sleeps well this night. The infusion is repeated on the third hospital day, and on this day practically all the symptoms have disappeared. The average requirement of whisky for satisfaction has been about 3 ounces (90 cc.) from admission to the disappearance of all symptoms. Convalescence from this point is uneventful. The authors base this treatment on their belief that alcoholism is a disease with a chronic progressive pathologic background characterized by successive acute pathophysiologic episodes which have primarily a nutritional background. The procedure requires careful, intelligent nursing and medical care if complications (insulin reactions, shocks) are to be minimized. The majority of the patients have liked the procedure, feeling that it has accomplished its purpose quickly and easily, as the fact that so many readmit themselves voluntarily bears out.

Journal of Pediatrics, St. Louis 17:423-570 (Oct.) 1940

- *Sulfathiazole in Treatment of Pneumonia in Infants and Children: Report on 167 Patients Treated with Sulfathiazole and a Comparison with 93 Patients Treated with Sulfapyridine. J. P. Scott, Philadelphia, and A. M. Jones, Memphis, Tenn.—p. 423.
 Evaluation of Enzyme Treated Milk in Infant Feeding. M. L. Blatt, E. H. Harris, H. M. Jacobs and Mary Zeldes, Chicago.—p. 435.
 Prothrombin in the Newborn Infant: Relationship to Maternal Dietary Vitamin K Intake. S. Kove and H. Siegel, Brooklyn.—p. 448.
 Recurrent Vomiting in Children: Factor of Food Hypersensitiveness. J. H. Fries and K. G. Jennings, Brooklyn.—p. 458.
 Study of Nutritional and Physical Status and Response to Exercise of Sixteen Negro Boys 13 to 17 Years of Age. F. W. Schlutz, Minerva, Morse, D. E. Cassels and L. Vivian Job, Chicago.—p. 466.
 Tuberculin Testing as Case-Finding Procedure. P. S. Phelps, V. P. Cenci and Alice Lawton, Hartford, Conn.—p. 481.
 Complications of Meckel's Diverticulum in Infancy and Childhood, with Analysis of Fourteen Cases. M. W. Everhart, New Orleans.—p. 483.
 *Duration of Benzdrine Sulfate in Management of Obesity in Children. R. H. Kunstadter, Chicago.—p. 490.
 Experience with Benzdrine Sulfate in Management of Obesity in Children. R. H. Kunstadter, Chicago.—p. 490.
 Relation of Vitamin D Intake to the Age of the Infant at the Time of Eruption of the First Deciduous Incisor. T. D. Speidel and Elizabeth Stearns, Iowa City.—p. 506.
 Teratoma of Pineal Body. J. R. Gerstley, J. Kasanin and Elizabeth Lowenhaupt, Chicago.—p. 512.
 Bronchiogenic Carcinoma of Seven Years' Duration in 11 Year Old Boy. M. G. Wasch, M. Lederer and B. S. Epstein, Brooklyn.—p. 521.
 Health Program for the Staff of a Children's Hospital. H. H. Work Jr., East Providence, R. I.—p. 529.

Sulfathiazole for Pneumonia in Children.—Scott and Jones report on the treatment with sulfathiazole of 167 infants and children having pneumonia and on 93 treated with sulfapyridine. The usual daily sulfathiazole dose was 1 grain (0.065 Gm.) per pound of body weight. From one fourth to one half of this amount was given as an initial dose, followed by one eighth of the daily dose every three hours throughout day and night and continued until the temperature had been normal for forty-eight hours. Oxygen, transfusion, enemas, measures to combat distention and to secure a free nasal airway, incision of eardrums, aural instillations and sponging were used when indicated. Between Oct. 1, 1938, and June 1, 1939, 58 of the patients treated with sulfapyridine received daily 1½ grains (0.1 Gm.) of the drug per pound of body weight. The remaining 35 patients treated in the fall of 1939 usually received 1 grain. Sulfathiazole seemed to precipitate an early crisis similar in character to the natural crisis to that produced by specific serum or to that produced by sulfapyridine. Usually within twelve hours the fever and toxicity lessened, dyspnea was relieved and the patient began to feel better. In many cases the temperature became permanently normal in twenty-four hours. After forty-eight hours few of the patients had fever and after seventy-two hours only 19 of 158 patients successfully treated had fever. Coincident with the fall in temperature, the child's appetite improved, and activity and responsiveness returned. In a few cases listlessness did not disappear until the drug was stopped in spite of other improvement. Usually physical pulmonary signs improved when the fever abated, but great variability was noticed in this clearing, as it is after a natural crisis. Five of the patients given sulfathiazole died. In the 158 cases in which satisfactory results were obtained, the time between the beginning of treatment and the beginning of a permanent normal temperature averaged 1.8 days. Diagnosis of bronchopneumonia was made

and confirmed by roentgen examination in 18 cases, in which the average days of fever was 1.62, as compared to 1.8 days for the whole group. A study of the time elapsing between the first dose of the drug and the return of temperature to normal of the patients treated with sulfapyridine shows that one cannot infer that there is any superiority of one drug over the other in this respect. Toxic effects following sulfathiazole were largely gastrointestinal, consisting of vomiting and diarrhea, and were mild in comparison with those caused by sulfapyridine. Sulfathiazole is easy to administer to young children and infants.

Duration of Diphtheria Immunity.—Christie presents data of a follow-up study on the lasting effect of seven antigens used for diphtheria immunity. The interval between doses was only one week and the interval after immunization to Schick tests was only three months. The author realizes the discrepancies but believes that they do not minimize the lesson to be learned from an accumulation of such data. Between July 1930 and October 1931 toxin antitoxin was used on 52 children. Three 1 cc. doses of the material were given at weekly intervals. After three months Schick tests revealed that 77 per cent of the children were Schick negative. Nine of this Schick-negative group were retested nine years later and 8 were still negative. Three weekly doses of 1 cc. of toxoid to which 0.5 per cent of alum had been added and contained a flocculating unitage of from 5 to 6 units per cubic centimeter were given 49 children. In three months 93 per cent of these children were Schick negative. Fourteen of them were retested seven years later and 12 (85 per cent) were still negative. Essentially the same material, except for a higher flocculating unitage, was given in two 0.5 cc. doses to 167 children one week apart. Ninety-one per cent of these were Schick negative, while after five and one half to seven years only 52 per cent of the 44 retested were Schick negative. Between August 1932 and April 1934 plain toxoid was given to 87 children with an initial dose of 0.5 cc. followed in one week by 1 cc. After one month 87 per cent of the group had a negative Schick reaction, after five and one half to seven years 8 of the 16 retested had become Schick positive. After one dose of alum-precipitated toxoid 90 per cent of 49 children were immunized but only 46 per cent of 13 retested after five years remained so. Another preparation was given in the same manner to 101 children (one dose of 0.5 cc.) but with a flocculating unitage three and one half times that of the preceding preparation. After six weeks 95 per cent of these children were Schick negative and after four years 75 per cent of 24 negative Schick reactors retested were still negative. Two 1 cc. doses of plain toxoid one week apart produced 94 per cent negative Schick reactors among 94 children in six weeks and after four years 75 per cent of the 24 retested were still negative.

Missouri State Medical Assn. Journal, St. Louis

37:455-490 (Nov.) 1940

- Coronary Vascular Disease. J. H. Musser, New Orleans.—p. 455.
Treatment of Nephritis by Rest. T. Addis, San Francisco.—p. 458.
Hyperthyroidism: Some Hazards in Surgical Treatment. E. V. Mastin, St. Louis.—p. 460.
Pneumococcal Pneumonia: Observations on Incidence and Therapy in St. Louis Area, 1939-1940. L. D. Thompson, L. L. Terry and J. C. Edwards, St. Louis.—p. 463.
Clinical Gastroscopy with Findings in 356 Examinations. B. Kenamore and H. Scheff, St. Louis.—p. 469.
Medical Care of the Old Aged Patient. C. E. Henry, Kirksville.—p. 471.
*Sulfanilamide Implantation as Method of Controlling Infection in Clean Surgical Wounds. M. A. Casberg, St. Louis.—p. 473.
Ketosis Simulating Acute Conditions of Abdomen. J. G. Probst and N. W. Drey, St. Louis.—p. 475.
Is Dentition an Etiologic Factor in Organic as Well as Functional Derangement of Infants? C. B. Summers, Kansas City.—p. 478.
The Relationship of Physicians and Dentists. A. O. Gruebbel, Jefferson City.—p. 480.

Sulfanilamide Implantation in Clean Surgical Wounds.

—Casberg used sulfanilamide crystals locally as prophylaxis against infection of clean wounds following inguinal herniorrhaphy. Two comparable groups of cases were used as controls. All the operations were performed during December, January and February, as in previous years wound infections were highest

during these months. From 6 to 8 Gm. of sulfanilamide was sprinkled into the subcutaneous tissues between the skin and the aponeurosis of the external oblique muscle. There were no postoperative wound infections among the 18 patients thus treated. Two infections occurred among the 19 patients of one control group and three among 25 of another control group. Three of the infections were due to *Staphylococcus aureus* and 2 to *Streptococcus haemolyticus*. The absence of wound infection following local sulfanilamide implantation does not obviate any of the operating room rules of asepsis.

Nebraska State Medical Journal, Lincoln

25:357-392 (Oct.) 1940

- Management of Ocular Trauma. T. E. Sanders, St. Louis.—p. 357.
Use of Sulfocyanates in Arterial Hypertension. G. W. Covey, Lincoln.—p. 363.
Delirium and Its Management. G. A. Young and R. H. Young, Omaha.—p. 370.
Study of 100 Sterile Marriages. L. S. McGoogan, Omaha.—p. 375.
Cancer of Tonsil. L. P. Coakley, Omaha.—p. 379.

New England Journal of Medicine, Boston

223:651-694 (Oct. 24) 1940

- Observations on Epidemiology of the Common Cold. W. G. Smillie, New York.—p. 651.
Relation of Sinusitis to Chronic Nontuberculous Chest Infection. R. L. Goodale, Boston.—p. 654.
Pathogenesis of Primary and Reinfection Types of Pulmonary Tuberculosis. E. R. Long, Philadelphia.—p. 656.
Treatment of Pneumococcal Pneumonia. F. G. Blake, New Haven, Conn.—p. 661.
Osteomyelitis of Coccyx and Sacrum with Sinus Formation Simulating Anorectal Fistula: Report of Two Cases. H. E. Bacon and A. Taylor, Philadelphia.—p. 668.
Emergency Treatment of Fractures. H. C. Marble, Boston.—p. 672.

New Jersey Medical Society Journal, Trenton

37:487-528 (Oct.) 1940

- Preventive Medicine in Modern Industry. E. E. Evans, Penns Grove.—p. 492.
Lame Back. F. R. Ober, Boston.—p. 501.
Treatment of Alcoholism. M. Moore, Boston.—p. 509.

North Carolina Medical Journal, Winston-Salem

1:523-578 (Oct.) 1940

- What Moves Man? J. K. Hall, Richmond, Va.—p. 523.
A Quarter-Century of Health Progress in North Carolina. R. Norton, Chapel Hill.—p. 529.
Carcinoma of Cervical Stump: Study of Incidence in a Series of Patients with Cervical Carcinoma Seen in North Carolina. R. L. Pearse, Durham.—p. 534.
Diabetes Mellitus. L. A. Crowell Jr., Lincolnton.—p. 538.
Sulfapyridine Therapy in Lobar Pneumonia, with Special Attention to Complications. E. E. McClure, G. Watson and W. R. Stanford, Durham.—p. 543.
Diagnosis and Management of Chronic Eczematoid Dermatitis of Hands. J. L. Callaway and S. W. Barefoot, Durham.—p. 547.
Experiences with Histaminase (Torantil): Preliminary Report. T. W. Baker, Charlotte.—p. 551.
Another Goiter Region. R. O. Jones, Burnsville.—p. 556.

Northwest Medicine, Seattle

39:351-392 (Oct.) 1940

- *Zinc Peroxide in Treatment of Surgical Infections. J. A. Gius, Portland, Ore.—p. 354.
Obstructive Jaundice: Its Surgical Consideration. V. C. Hunt, Los Angeles.—p. 358.
Relapsing Fever. M. W. Hemingway, R. W. Hemingway and V. K. Arneson, Bend, Ore.—p. 362.
Treatment with Vitamins. D. L. Wilbur, San Francisco.—p. 364.
Education of the Acoustically Handicapped. Elvena Miller, Seattle.—p. 369.

Zinc Peroxide for Surgical Infections.—Gius reports four cases in which zinc peroxide was used with good results in three, while the fourth illustrates a hazard of introducing zinc peroxide or similar material into a closed cavity. In the first three cases the infection was localized to the parietes, but in the fourth case it was confined to the pelvis and zinc peroxide could be introduced only by injection through the colpotomy wound. The zinc peroxide suspension passed through the wall of the abscess and into the peritoneal cavity, resulting in diffuse peritonitis. Fortunately, the patient recovered and has apparently been cured.

Ohio State Medical Journal, Columbus

36:1037-1144 (Oct.) 1940

- Brucellosis (Undulant Fever). W. M. Simpson, Dayton.—p. 1053.
 Role of Intubation in Treatment of Intestinal Obstruction. W. O. Abbott, Philadelphia.—p. 1061.
 Brief Summary of Malignant Neoplasms Proved at Autopsy Which Simulated Pulmonary Tuberculosis. R. J. Ritterhoff, Cincinnati.—p. 1066.
 Eye Affections Secondary to General Diseases. E. J. Wenaas, Youngstown.—p. 1068.
 Care of the Newborn. M. L. Ainsworth, Columbus.—p. 1073.
 Blood Dyscrasias of Infancy and Childhood. H. Wellmeier, Piqua.—p. 1078.
 Clinical Study of Intestinal Parasites. H. H. Ingling, Springfield.—p. 1083.
 Consideration of Some Causes of Increased Intracranial Pressure. J. P. Evans, Cincinnati.—p. 1086.
 Splenomegaly and Hepatic Enlargement Apparently Relieved by Injections of Spleen Fluid: Report of Case. G. A. Hoke, Elyria.—p. 1090.
 Some Errors and Misconceptions in Clinical Endocrinology. A. G. Sar-Louis, Cleveland.—p. 1092.
 Acute Chest Conditions in Children. W. B. Taggart, Dayton.—p. 1096.

36:1145-1248 (Nov.) 1940

- Facts and Fiction About Our State Hospitals. W. Overholser, Washington, D. C.—p. 1161.
 Diagnosis and Significance of Tuberculous Infection. J. H. Skavlem, Cincinnati.—p. 1168.
 Minor Discomforts of Pregnancy. F. W. Davis, Columbus.—p. 1174.
 Vaginalpelvic Massage and Tamponade: Conservative Gynecologic Procedure. C. J. Vogt, Cleveland.—p. 1178.
 Symmetrical Cerebral Calcification Simulating Brain Tumor. A. T. Steegmann, Cleveland.—p. 1181.
 Acute Respiratory Emergencies. S. C. Yinger, Springfield.—p. 1185.
 Ophthalmoscopic Interpretation of Retinal Vascular Disease. W. F. Hatcher, Youngstown.—p. 1190.
 Urban Safeguards Against Milk-Borne Diseases. H. J. Knapp, Cleveland.—p. 1191.
 Roentgen Kymography in Study of the Heart in Childhood. J. V. Greenebaum, S. Brown and T. Selkirk, Cincinnati.—p. 1194.
 Acute Cholecystitis. R. C. Austin, Dayton.—p. 1198.
 Immediately Preoperative, Fatal Pulmonary Embolus. R. R. Renner and K. S. Russell, Cleveland.—p. 1201.

Pennsylvania Medical Journal, Harrisburg

44:1-128 (Oct.) 1940

- Lest We Forget: Presidential Address. F. F. Borzell, Philadelphia.—p. 13.
 *Clinical Report of Epidemic of Acute Infectious Jaundice. B. G. Learn, Blandburg.—p. 18.
 Spontaneous Expulsion of Submucous Lipoma of Cecum. G. S. Backenstoe, Emmaus.—p. 21.
 The Hospital's Personality and Environment. B. Gordon, Philadelphia.—p. 23.
 Role of Infection in Kidney Disease. J. A. Kolmer, Philadelphia.—p. 26.
 Subtotal Gastrectomy for Peptic Ulcer. W. T. Lemmon, Philadelphia.—p. 31.
 Chronic Adult Tetany of Gastrointestinal Origin: Treatment with Dihydratichysterol: Report of Case. V. W. Eisenstein, Pittsburgh.—p. 33.
 Treatment of Tetany with Dihydratichysterol. T. C. Wilkinson, Pittsburgh.—p. 37.
 Diabetes: VI. Diabetic Diets and Eating Habits of Nationalities. A. L. Luchi, Wilkes-Barre.—p. 41.
 Indirect Blood Transfusion: Simplified Method: Report of 196 Cases. S. A. Rosenberg and H. J. Bayer, Pittsburgh.—p. 45.
 Staphylococic Septicemia Coexisting with Diabetes: Report of Case with Recovery. H. H. Seiple, Lancaster.—p. 50.

Epidemic of Acute Infectious Jaundice.—Learn discusses sixty-two instances of epidemic acute infectious jaundice encountered in his private practice. The cases began to appear in September 1937 and continued to March 1938; no more cases were observed until September 1938, when the epidemic again became prevalent and lasted until March 1939. Since that time only three cases have been observed. Most of these cases were mild and ambulatory; the greatest number occurred in children from 6 to 8 years of age. The youngest patient was 3 and the oldest 47 years of age. The severity of the illness usually increased with the age of the patient. The incubation period was two weeks in most of the cases. As many as six cases occurred in one family, but not all the exposed children were affected. Clinical evidence shows that the disease is transmitted from person to person and that most adults are immune. There were few complications and only one death in the author's series. Epigastric pain, nausea, fever and tenderness in the upper right quadrant occurred in all the cases, vomiting in forty-seven, bile in the urine in thirty-six cases, clay-colored stools in eighteen and epistaxis in twelve. A spirochete which resembles *Leptospira* was isolated in a sufficient number of the cases to determine that it was the cause of the epidemic. In two of the three

cases in which there was a recurrence of the jaundice the dark-field examination was positive. In one of these the spirochetes were recovered from the macerated kidney substance of an inoculated guinea pig.

Public Health Reports, Washington, D. C.

55:1879-1932 (Oct. 18) 1940

- Housing Problem as It Affects Public Health Nursing Activities. Mary J. Dunn.—p. 1879.
 Sanitary and Physiologic Aspects of Flooring Materials. J. M. DallaValle.—p. 1884.
 Studies on Duration of Disabling Sickness: I. Duration of Disability from Sickness and Nonindustrial Injuries Among the Male and Female Memberships of Twenty-Five Industrial Sick Benefit Organizations, 1935-1937, Inclusive. W. M. Gafafer and Elizabeth S. Fraser.—p. 1892.
 Rheumatic Fever in New Haven, Conn.: Survey of Recent Hospital Admissions. Lucille R. Farquhar and J. R. Paul.—p. 1903.

55:1933-1976 (Oct. 25) 1940

- *Institutional Outbreak of Pneumonitis: I. Epidemiologic and Clinical Studies. J. W. Hornbrook and K. R. Nelson.—p. 1936.
 *Id.: II. Isolation and Identification of Causative Agents. R. E. Dyer, N. H. Topping and I. A. Bengtson.—p. 1945.
 *Relation of Body Build to Drug Addiction. R. R. Brown.—p. 1954.

Institutional Outbreak of Pneumonitis.—According to Hornbrook and Nelson, 15 cases of pneumonitis occurred during the spring of 1940 among the 153 employees in one building of the National Institute of Health. The roentgenograms of the cases showed one or more pneumonic shadows. There were a few other cases of a somewhat similar but milder type which gave no roentgen signs or roentgenograms were not obtained. The onset was fairly sudden though usually not severe. Two types of onset predominated, one coryza-like, the other with headache, chilly sensations and general malaise. There was a latent period of about three days following the onset in which the patient continued to work although feeling ill. Severe and persistent headache was a prominent symptom developing during the latent period. In none of the cases was a "prune juice," rusty or blood-tinged sputum observed. Approximately half of the patients developed vague neuralgic chest pains in the substernal region or on the side of their demonstrated pulmonary lesion. All the patients complained of insomnia. There were no physical abnormalities on physical examination; in fact, their absence was one of the characteristics of the disease. On admission the average pulse rate was 99 beats and the average temperature was 102.4 F. (varying from 100.5 to 104.5 F.). The pulse rate did not always parallel the temperature curve. The roentgen examination gave the most typical and consistent evidence of pulmonary lesions. A soft infiltrative lesion, single or multiple, was visible on the films but was not of the uniform density seen in lobar pneumonia. The lesions appeared to be more of the patchy type seen in bronchopneumonia. It is doubtful whether many of the patients would have been considered as having a pneumonic process without roentgen examination. Blood cultures, agglutination tests, using *Eberthella typhi*, *Brucella abortus*, *Bacillus proteus* OX19 and *Pasteurella tularensis* as antigens, and sputum studies for pneumococci were negative. The usual supportive hospital treatment was given all the patients. Other than 1 death there were no serious complications. Dyer and his co-workers isolated the etiologic organism, the rickettsia of Q fever, from 3 of 4 of the epidemic cases in which it was attempted. From various reports by other workers it seems possible that this disease has had a widespread geographic distribution; the cases of these other outbreaks have been reported as bronchopneumonia of unknown etiology (variety X), atypical pneumonia and atypical bronchopneumonia. The clinical course of these outbreaks and of the epidemic under discussion was consistent. The three strains isolated gave cross immunity to one another, to strain of American Q fever previously reported from the laboratory of the National Institute of Health as "strain X" and to a strain of Australian Q fever received from Burnet. Dyer and his co-workers point out that no valid evidence was adduced that personal contact or the intervention of an arthropod vector was responsible for the transmission of the disease. Strains of Q fever have been carried in animals and tissue cultures in one unit of the National Institute of Health since 1938. Whether or not this unit served as a source of infection is open to question, since the personnel of the unit was spared and the cases were widely distributed throughout the building.

Body Build and Drug Addiction.—Brown made anthropometric studies of 400 native white male adult addicts following their admission to the United States Penitentiary Annex, Fort Leavenworth, Kansas. The cases represented consecutive admissions, the only selecting factors being those of color, nativity and verified history of drug usage. Measurements were taken on unclothed patients according to the technic of Hrdlicka. Subjective estimates were made also of the face shape, face profile, conformation of head, baldness, neck, trunk profile, general appearance as to nutrition, skin color, musculature, dysplastic traits and estimate of body type. On the basis of the investigation the narcotic drug addicts of the study were average or slightly superior in height and weight. There was an average gain in weight of a little more than 3 Kg. (6½ pounds) after five and a half months of institutionalization. The body build of the group was found to be within normal limits with a trend toward the pyknic end of the distribution. The drug addiction of the group could not be ascribed to gross constitutional weakness.

Southwestern Medicine, El Paso, Texas

24:319-356 (Oct.) 1940

Cancer of Small and of Large Intestines. J. S. Horsley, Richmond, Va. —p. 319.

*Necessity for Accuracy and Simplification in Diagnosis of Renal Tuberculosis. J. L. Emmett, Rochester, Minn.—p. 324.

Relation of Psychiatry to Other Departments of Medical Practice. S. D. Ingham, Los Angeles.—p. 331.

Bronchial Obstruction. T. H. Bate, Phoenix, Ariz. p. 336.

Retention Catheter Treatment of Vesicovaginal Fistula. R. F. Thompson, El Paso, Texas.—p. 338.

Abdominal Surgical Emergencies. E. P. Palmer, Phoenix, Ariz.—p. 340.

Diagnosis of Renal Tuberculosis.—Emmett points out that in the diagnosis of renal tuberculosis the trend is away from retrograde pyelography and toward excretory urography. There are only four methods of investigating a kidney in the presence of tuberculous disease, and all may give negative results even though tuberculosis is present. These methods are urography, determination of pus corpuscles in a "wet smear" of urine obtained by ureteral catheterization, microscopic examination of a stained specimen of ureteral urine for acid-fast bacilli, and inoculation of guinea pigs with a catheterized specimen of urine. All these examinations except descending urography require cystoscopic investigation. More than one cystoscopy may be required to make all of them. Cystoscopy carried out in the presence of urinary tuberculosis is usually a painful procedure unless anesthesia is employed. Repeated cystoscopy is not only painful but it may traumatize infected tissue. Only those examinations should be employed which enable one to arrive at a sound diagnosis. The ultimate in diagnosis in renal tuberculosis is the minimal amount of investigation that will permit a diagnosis sufficiently accurate to suggest correct treatment. One brief cystoscopic examination should be sufficient in each case. Repeated instrumentation is to be avoided. The excretory urogram will indicate the involved kidney in most cases and it is accurate in this regard. The excretory urogram will suggest the condition of the uninvolved kidney, but this information is inaccurate and must be supplemented by an examination of a ureteral specimen of urine, by microscopic examination of the wet smear, special staining methods for acid-fast organisms and inoculation of guinea pigs with specimens of urine. Retrograde pyelography is rarely necessary for the involved kidney but is occasionally necessary for the uninvolved kidney when the excretory urogram is poor. Routine bilateral pyelograms are entirely unnecessary and are not in the interest of the patient either economically or physically. They may be necessary in a small group of cases in which the diagnosis is in doubt. The results of nephrectomy in 1,131 cases of renal tuberculosis performed at the clinic between 1912 and 1932 indicate that the term "unilateral" renal tuberculosis is not justified. They demonstrate that the more nearly "normal" the uninvolved or the least involved kidney is proved to be, the better will be the clinical results following removal of the involved kidney. The results of nephrectomy in grossly bilateral renal tuberculosis are not good and do not justify its performance on the belief that removal of the worse kidney may relieve the vesical symptoms. Of 718 cases in which the specimen of urine from the uninvolved kidney contained no pus corpuscles, 65.2 per cent of the patients were either cured or improved at the end of five years and

56.4 per cent at the end of ten years. Among these cases there were 55 in which inoculation of guinea pigs with urine gave positive results, and only 36.4 per cent of these patients were cured or improved at the end of five years and only 30 per cent were alive at the end of ten years. The best results were obtained among 209 patients in whom no pus corpuscles were being excreted from the uninvolved kidney and the results of inoculation of animals with specimens of ureteral urine were negative. At the end of five years 75.2 per cent of the patients were cured or improved and at the end of ten years the percentage was 65.5.

Surgery, Gynecology and Obstetrics, Chicago

71:569-696 (Nov.) 1940

*Blood and Lymph Vessel Tumors: Report of 1,056 Cases. W. L. Watson and W. D. McCarthy, New York. p. 569.

*Acute Intestinal Obstruction. C. W. Mayo, J. M. Miller and L. K. Staffer, Rochester, Minn. p. 589.

Reaction of Bone to Multiple Metallic Implants. R. T. Bothe, L. E. Benton and H. A. Davenport, Chicago. p. 598.

*Ivy Bleeding Time, Serum Volume Index and Prothrombin Content of Blood in Estimating Bleeding Tendency in Jaundice. L. K. Ferguson, D. G. Calder Jr. and J. G. Reinhold, Philadelphia. p. 603.

Perforated Peptic Ulcer: More Accurate Method of Roentgen Diagnosis. A. J. Williams and H. V. Hartzell, San Francisco. p. 606.

Pregnancy and Experimental Pulmonary Tuberculosis in Rabbits. H. E. Burke, Ray Brook, N. Y. p. 615.

Pharmacodynamic Effects of Certain Oxytocics on Tonal Contractions in Rhesus Monkey. A. H. Morse, New Haven, Conn., and I. C. Rubin, New York.—p. 626.

Resection of Portion of Thoracic Esophagus for Carcinoma: Report of Two Cases. R. N. Carter, Cincinnati. p. 624.

Head Injury Survey. H. V. Bensen, Los Angeles. p. 633.

Fractures in Region of Elbow in Children: End-Result Study. A. H. Brewster and M. Katz, Boston. —p. 633.

Multiple Primary Carcinoma. O. F. Larson, Seattle. p. 650.

Essential Problems in Surgical Treatment of Inguinal Hernia. L. M. Zimmerman, Chicago. p. 654.

Treatment of Cervical Nodes in Intra-Oral Cancer. J. J. Duffy, New York.—p. 664.

Extraperitoneal Method of Repairing Third Degree Prolapse of Sigmoid Following Colostomy. J. R. Veal, Washington, D. C. p. 672.

Gas Cysts of Intestine. J. A. Jackson, Madison, Wis. p. 675.

Injury to Femoral Articular Cartilage by Medial Meniscus. A. J. Smith and R. B. King, New York. p. 679.

Blood and Lymph Vessel Tumors.—Watson and McCarthy made a study of 1,056 patients with 1,363 benign lymph and blood vessel tumors admitted to the Memorial Hospital during 1931 to 1939. There were 1,308 hemangiomas, 41 lymphangiomas and 14 hygromas. Seventy-three per cent of the patients presented evidence of tumor at birth and 85 per cent developed before the end of the first year. The authors propose a classification based on clinical, pathologic and therapeutic considerations: capillary hemangioma, cavernous hemangioma, angioloblastic or hypertrophic hemangioma, racemose hemangioma, diffuse systemic hemangioma, metastasizing hemangioma, naevus vinosus or port wine stain, and hereditary hemorrhagic telangiectasis (Rendu-Osler-Weber disease). Solid carbon dioxide was satisfactory for superficial capillary lesions and for clearing the residual mottled areas remaining after sodium morrhuate therapy. Sodium morrhuate injection was most effective for simple cavernous and stellate hemangiomas and for Rendu-Osler-Weber disease. Solid carbon dioxide and sodium morrhuate were used together or combined with radiation. External radium brass applicators were especially applicable for capillary hemangiomas that were too thick for solid carbon dioxide therapy and also for superficial small cavernous hemangiomas resistant to sodium morrhuate. Interstitial irradiation, radon-filled, hollow 4 mm. gold seeds, was reserved for the most resistant hemangiomas and was especially well adapted for thick, bulky capillary or cavernous hemangiomas requiring skin damaging doses of external radiation. Gold radon seeds were employed for rapidly growing hemangiomas resistant to sodium morrhuate and as an adjunct for racemose angiomas. The end results obtained with high, medium and low voltage roentgen rays were disappointing. However, high voltage roentgen therapy seems indicated for osseous, large hepatic cavernous hemangiomas, hemangiomas of joints, synovia, inoperable extensive muscle angiomas and certain racemose hemangiomas. There is no successful treatment for metastasizing hemangioma. More good regressions were obtained in infants less than 3 months of age than in those more than 6 months of age. Radiation measures are hazardous and should be used with caution for hemangio-

mas of the scalp, midline areas over the sternum or vertebrae, breasts, genitalia, long bones, lips and areas adjacent to the eyes. Surgical excision is indicated for the small papillar tumors, bulky capillary lesions in areas where scars may be concealed, the resistant angioliomas, muscle hemangiomas and angiofibromas. Port wine stains do not respond well to radiation, solid carbon dioxide or sodium morrhuate. Small lesions may be excised, but larger ones can be improved cosmetically only by covering them with cosmetic paste. The percentage of good results for surgical excision was 91, for solid carbon dioxide 88, for sodium morrhuate 86, for a combination of the latter two measures 86, for combined radiation and physical methods 65, for external radon radiation 61, for interstitial radon radiation 59, for "x-radiation" 48 and for combined radiation 57. Lymphangiomas, like hemangiomas, may possess marked growth capacity and are not, as was once supposed, dilated, static, normal lymph channels. Of the 41 lymphangiomas 61 per cent were present at birth and 95 per cent were observed before the age of 10. The lymphangiomas have been classified into five divisions: simple, cavernous, cellular or hypertrophic, diffuse systemic lymphangiomas and cystic hygroma or the cystic lymphangioma. The tumor definitely develops from lymphatic tissue in the neck, axilla, retroperitoneal tissues or groin. Hygromas are generally present at birth and grow rapidly. Thirteen of the 14 tumors were located in the neck and the other one in the axilla. Wide surgical excision affords the best prognosis in the treatment of lymphangiomas despite unsightly scars and postoperative keloids. The operative results were good in 77 per cent of 13 patients. Lymphangiomas are radioresistant. However, irradiation is the method for diffuse systemic lymphangiomas which affect an entire extremity. Sodium morrhuate injections have no effect on lymphangioma, with the exception of cystic hygroma. Seventeen lymphangiomas recurred. Cystic lymphangiomas (hygromas) are relatively radioresistant. Surgical excision was performed in 7 cases with a good result in 5. Sodium morrhuate should be tried for all hygromas and if it fails, surgical excision should be tried, and if excision is incomplete then irradiation may be attempted.

Acute Intestinal Obstruction.—Mayo and his associates point out that the mortality from acute intestinal obstruction continues despite improvements in surgical technic and added therapeutic aids. Bands and adhesions, congenital or inflammatory, are second only to external hernias as causes of intestinal obstruction. Twenty-four patients suffering from acute intestinal obstruction as a result of bands and adhesions were seen at the Mayo Clinic from 1935 to 1939, during which time 136 cases of acute intestinal obstruction were encountered. Of these 136 cases 81 were due to external hernias. Internal hernias as a result of abdominal operations are less frequent, owing to operative precautions, such as the suturing of the stomach to the opening in the transverse mesocolon when posterior gastro-enterostomy is performed. The more important internal hernias at present are those resulting from congenital defects. Seven cases of internal hernias and acute intestinal obstruction were seen at the clinic during the five years under consideration. Volvulus of various portions of the intestinal tract accounted for only 9 acute intestinal obstructions. Intussusception accounted for 10 cases; 8 of the patients were 2 or less years of age, 1 was 4 and 1 was 6. Three of the cases were caused by mesenteric thrombosis, 2 were due to gallstones, 2 to congenital mesenteric cysts, 2 to diverticulitis and 4 to carcinoma. Simple mechanical obstructions of the small intestine early in the postoperative period in which strangulating lesions can be eliminated respond well to decompression of the intestine by the Wangenstein method. This is not true for obstructions of the small intestine caused by bands and adhesions in the late postoperative period. Analysis of the results of this group reveals a high incidence of strangulation. Signs indicative of strangulation must be watched for and, if not present, conservative treatment may be employed. Colonic obstruction must be considered a strict contraindication to the use of suction drainage. Cecostomy or colostomy is the procedure of choice and does not carry an elevated risk in comparison with "blind" intubation. When operation is indicated, the most conservative procedure possible under the exist-

ing circumstances should be employed after the patient has been properly prepared. When resection is necessary, the loop should be exteriorized and the continuity of the intestine restored later when the patient is in better condition. Primary resection with closure of the intestine and side to side anastomosis is too hazardous a procedure unless performed for a small lesion high in the intestine. Useful postoperative therapeutic adjuncts are blood transfusions and 100 per cent oxygen. There is a correlation between the duration of obstruction or strangulation and the mortality rate. The combined mortality among the 136 patients was 22 per cent and of the patients who died about half had been ill for more than forty-eight hours before coming to operation and an additional 3 had been ill about forty-eight hours. The adverse effect of delay in recognizing and treating strangulating lesions is especially true in obstructions caused by bands and adhesions in the late postoperative period. The prophylactic repair of hernias in suitable cases will reduce not only the incidence of obstruction but also the resultant mortality rate.

Tests Estimating Bleeding Tendency in Jaundice.—Ferguson and his associates performed simultaneously the Ivy bleeding time test, the serum volume test of Boyce and McFetridge and the Quick method of determining the prothrombin content of the blood. The estimations were made from the same specimen of blood drawn from each of 27 jaundiced patients. The jaundice was due to various causes. The authors find that there is sufficient correlation between the tests to warrant confidence in the use of the two simpler tests as adjuncts to or substitutes for prothrombin studies or when laboratory facilities for prothrombin determination are not available. A blood prothrombin level of 30 per cent or less was selected arbitrarily as a level at which danger of bleeding due to prothrombin lack was imminent. Of nine determinations in which the prothrombin percentage was 30 per cent or less either the Ivy bleeding time or the serum volume index or both indicated a definite bleeding tendency. In 2 cases in which the prothrombin percentage was respectively 33 and 50 per cent, a definite hemorrhagic tendency was suggested by the Ivy bleeding test, the serum volume index and clinical evidence of bleeding. In a third case with a prothrombin determination of 30 the serum volume index was 0.76, not indicative of a bleeding tendency, though the Ivy bleeding time was ten minutes. In none of the cases with a prothrombin percentage above 30 was there clinical evidence of bleeding. Seven of these patients showed a serum volume index between 0.7 and 0.8 and in 3 of these the Ivy bleeding time indicated a bleeding tendency and in 1 the serum volume index was reduced to a definitely critical level. However, in no case did both tests indicate a definite hemorrhagic tendency, although in 2 with the Ivy bleeding time prolonged the serum volume index was between 0.7 and 0.8. Therefore either one or both of the two simple tests showed the tendency to hemorrhage in cases in which it was indicated by the blood prothrombin level. In 2 cases both tests indicated the hemorrhagic tendency in agreement with the clinical evidence, while the prothrombin percentage did not. In 4 cases one or the other of the simpler tests indicated a hemorrhagic tendency when there was no other evidence that it existed.

Texas State Journal of Medicine, Fort Worth

36:401-462 (Oct.) 1940

- Anemias of the Newborn Period. B. Reading, Galveston.—p. 405.
Effect of Drugs on Hematopoietic System. M. D. Levy, Houston.—p. 410.
Biochemical Aspects of Hematology. M. Bodansky, Galveston.—p. 415.
X-Ray Treatment of Ewing's Tumor. R. H. Crockett, San Antonio.—p. 417.
Roentgen Diagnosis of Calcified Pelvic Tumors. C. A. Stevenson, Temple.—p. 422.
Some Epithelial Tumors of Eyelids and Their Management. S. K. Stroud and C. D. Stewart, Corpus Christi.—p. 426.
Anesthesia in Peroral Endoscopy. J. B. Nail, Wichita Falls.—p. 430.
Hypoid Bursitis. L. A. Nelson, Dallas.—p. 435.
Endocrine Factor in Dysfunction of Organs of Special Sense. H. L. Warwick, Fort Worth.—p. 438.
Activities of the Bureau of Food and Drugs of the Texas State Department of Health. F. D. Brock, Austin.—p. 440.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Edinburgh Medical Journal

47:645-716 (Oct.) 1940

Role of Zinc Ionization in Treatment of Allergy in Nose. J. F. Birrell.—p. 645.

Contributions of Genetics to Reconstructive Medicine. F. A. E. Crew.—p. 653.

Gas Warfare. J. Kendall.—p. 664.

Study on Allergy in Experimental Tuberculosis. C. Clayson.—p. 675.

Artificial Pneumoperitoneum Applied to Certain Therapeutic Problems in Pulmonary Tuberculosis. J. P. McIntyre.—p. 687.

Expectorants in Chronic Bronchitis. S. Alstead.—p. 693.

*Action of Acetylsalicylic Acid on Teeth. D. B. Dott.—p. 700.

Action of Acetylsalicylic Acid on Teeth.—Dott found that strong solutions of acetylsalicylic acid extract calcium from teeth. His observations leading to this observation were as follows: He dissolved 5 grains (0.32 Gm.) of acetylsalicylic acid in 1 ounce of distilled water at about 140 F. The solution was poured on four teeth in a 2 ounce bottle. This was gently rotated and the solution was quickly filtered after five minutes, and then ammonia and ammonium oxalate were added. There was an immediate white cloudiness soon settling as a definite precipitate. The teeth used appeared normal and free from carious matter. The experiment was repeated and the solution was left in contact with the teeth for ninety minutes before filtering and precipitating. The washed oxalate was dried and strongly ignited in a porcelain crucible, and the resulting calcium oxide weighed 0.011 Gm. (0.17 grain). In several other experiments it was found that the loss of weight of the teeth after the action of acetylsalicylic acid was much greater than the weight of calcium oxide obtained. By dissolving equal weights of acetylsalicylic acid and sodium bicarbonate, one obtains a faintly alkaline solution which has no appreciable action on teeth. The author points out that the question as to how far these facts should limit the use of acetylsalicylic acid as a mouth wash is for medical decision.

Glasgow Medical Journal

16:115-146 (Oct.) 1940

Analogy Between Intrinsic Muscles of Eye and Muscle of Heart. A. M. Ramsay.—p. 115.

Codeine in Chronic Bronchitis. S. Alstead.—p. 126.

Guy's Hospital Gazette, London

54:281-298 (Oct. 5) 1940

*Cerebrospinal Meningitis. N. Mutch.—p. 282.

*Insulin Substitutes—Résumé of Present Day Knowledge. G. R. W. N. Luntz.—p. 285.

Notes on Peripheral Nerve Injuries. R. H. Harley.—p. 288.

*Strangulated Inguinal Hernia in Child of 5 Weeks. J. Gordon.—p. 290.

Cerebrospinal Meningitis.—The only effective prophylaxis, according to Mutch, against cerebrospinal meningitis consists in free ventilation and the avoidance of overcrowding. Since the survival time of the isolated meningococcus is short, the disease can be contracted only by close association with some one already infected. It was found that the carrier rate of infection could be reduced in dormitories to 5 per cent by spacing beds 3 feet apart, compared with a 20 per cent rate in 1 foot bed interspacing and a 29 per cent rate in a 9 inch bed interspacing. In the treatment of cerebrospinal meningitis, lumbar puncture and antimeningococcus serum have been replaced by sulfanilamide and sulfapyridine with marked results. Here the superiority of one drug over the other has not yet been determined. In 5,306 cases notified during the war years of 1914-1918 mortality was as high as 65 per cent; in 5,093 cases reported for the first six months of 1940 the death rate was only 20 per cent. Lumbar puncture is performed only at weekly intervals or when definite signs of increased intracranial pressure are observed. The dosage, administered in approximately equal quantities for the two drugs, ranged from 3 Gm. in infants to 9 Gm. in adults (down to 15 years) and was given daily for a week in six doses spaced four hours apart in order to maintain a uniform concentration in the body tissues but allowed for adjustments in severe attacks with supplementary intravenous

injections of soluble sulfapyridine. Comatose patients were given the drug in powdered form in suspension through a stomach tube. Intramuscular injections were found impracticable for a number of reasons. In view of the frequent occurrence of adrenal hemorrhage in cases of septicemia rapidly terminating fatally, vitamin C, citrus fruits and adrenal cortex extract are tentatively suggested as means of saving life. Since rapid dehydration occurs in unconscious pyrexial patients, a copious fluid intake is recommended either by stomach or by rectal tube or by an intravenous drip of dextrose-saline solution. The author discusses the nature of the infective organism, its path of invasion, the spread of the infection, the clinical varieties of the disease and complications such as the common occurrence of arthritis. A preparation that is inexpensive, soluble and susceptible of being administered rectally to unconscious patients or to those with troublesome cerebral vomiting is a desideratum.

Insulin Substitutes.—Luntz summarizes present day knowledge of insulin substitutes. All of these aim at curing or alleviating diabetes by oral administration. However, no remedy replacing insulin for pancreatic dysfunction has yet been found. The use of substitutes not only delays initiation of proper medication but invites the progress of the disease to a dangerous stage. Improvement attributed to the oral use of substitutes is, in reality, due to the strict regimen imposed on the patient, as various investigations have shown. Substances employed as substitutes or experimented with include guanidine derivatives, succinic acid, a decoction of the kadal ranji root, a hypoglycemic extract of the roots of the "devil's club," duodenal extracts, vegetable protein preparations, protein injections and cabbage extracts. Guanidine derivatives are synthetic compounds with an effect resembling that of insulin. Used on the continent they have been found by British investigators to be impracticable and even dangerous. A continental product (synthalin), a decamethylene diguanidine hydrochloride and reported to lower blood sugar, did in some cases lower ketosis in the urine but also exhibited toxic properties by inducing gastrointestinal disturbances in many patients and jaundice and hepatitis in others. Synthalin is a harmful drug, as it lowers the blood sugar not by promoting increased oxidation of dextrose but by a toxic effect on the liver. Neosynthalin, containing fourteen methylene groups, appears to be less toxic and perhaps not so active as the original product. Succinic acid, orally administered for the control of diabetic ketosis, in the hands of English and Scotch analysts either gave negative results or failed to prevent the onset of diabetic coma or to diminish chronic diabetic ketonuria. Györgyi, its author, proceeded on the assumption that the C₄ carboxylic acids, especially pyruvic acid, played a vital part in intermediate carbohydrate metabolism and that ketosis represented a dysfunction of these acids and could be prevented by succinic acid (obtained from amber, COOH.CH₂.CH₂.COOH, containing four carbon atoms) acting as a catalyzer. The kadal ranji root decoction popularly used by Indians for diabetes, renders the urine of diabetic subjects sugar free by raising the renal threshold for the excretion of sugar. It is considered dangerous by its author. Investigations of the hypoglycemic substance inherent in the extracts from the devil's club root (*Fatasia horrida*) and ostensibly nontoxic is being further investigated. Duodenal extracts, first used in 1939, failed to give uniform clinical results. The extract varied in different cases, not in relation to the actual severity of the case, but rather to the duration of the disease. A diminution of hyperglycemia, glycosuria and diuresis and an increase in weight were noted. A vegetable protein preparation derived from the germ of the carob or locust bean (*Ceratonia siliqua*) and tried out on diabetic children yielded inconclusive results. Protein injections prepared by G. Singer merit further consideration, though his view that they form the basic treatment of diabetes cannot be accepted. The mechanism of action is by no means clearly understood. The effect on diabetes may be due to their power of modifying metabolism. Experiments with cabbage extracts on blood sugar concentration, with which MacDonald and Wislicki experimented on animals, chiefly rabbits, to discover a preparation devoid of toxic effects, yielded them both a hyperglycemic and a hypoglycemic fraction. The latter was effective orally as well as when injected and no hypoglycemic convulsions

were evoked. In a depancreatized dog which had been kept alive by injections of insulin, blood sugar and glycosuria were controlled by the sole use of this extract and insulin could be withdrawn entirely. A two day interval between withdrawal of the cabbage extract and resumption of insulin therapy was marked by an abrupt rise in the concentration of dextrose in the blood and urine. According to Luntz the specificity of insulin in the successful management of diabetes should constantly be emphasized against the proponents of all irrational medicines and therapies until a better remedy has been found. Synthetic products so far evolved cannot compare with insulin in efficacy and are of little if any use in the practical treatment of diabetes. The ultimate conquest of diabetes may depend on a more thorough understanding of carbohydrate metabolism. That implies a better understanding of the anterior pituitary, the adrenal cortex and various other active agents in the body.

Strangulated Inguinal Hernia in Infant.—Gordon reports the rare case of strangulation of congenital hernia in an infant aged 5 weeks, the third child born of a normal mother aged 26. At birth the mother had noticed a lump in the right groin, which, however, had disappeared a week later. The reappearance of this lump under circumstances of aggravated screams, bile-stained vomiting and attacks of colic caused the child to be hospitalized. The lump was found to be red, tense and irreducible. No right testis was found. The abdomen was distended with visible coils of intestine but with no visible peristalsis. There were no feces in the rectum. When the inguinal canal was opened a tense hernial sac was encountered, containing about 8 inches of blue ileum, 1 inch of which was plum colored. A tough constriction of the internal inguinal ring was divided, but as the child began to cry no resection of the intestine was attempted and no repair operation done to strengthen the inguinal sac. The child was given 20 ounces (600 cc.) of saline solution by subcutaneous drip during the first twelve hours after the operation and was then breast fed. The child continued to feed normally, no longer vomited, recovered stool action and was discharged six days later.

Journal of Hygiene, London

40:501-614 (Sept.) 1940

- Somatic Antigens of Clostridium Welchii Group of Organisms. D. W. Henderson.—p. 501.
Design and Significance of Synergic Action Tests. K. Mather.—p. 513.
Bismuth Sulfite Mediums for Isolation of Vibrio Cholerae. W. J. Wilson and L. V. Reilly.—p. 532.
Inheritance of Resistance, Demonstrated by Development of Strain of Mice Resistant to Experimental Inoculation with Bacterial Endotoxin. A. B. Hill, J. M. Hatswell and W. W. C. Topley.—p. 538.
Osmotic Pressure, After Resolution, of Serum Dried from Frozen State (F. D. Serum). G. S. Adair, Muriel E. Adair and R. I. N. Greaves.—p. 548.
Poisoning by 2-Methylbutyraldehyde (Isovaleraldehyde). J. F. Wilkinson.—p. 555.
Use of Hypochlorites for Aerial Disinfection. A. H. Baker, S. R. Finn and C. C. Twort.—p. 560.
Effects of Morphine, Diacetylmorphine and Some Related Alkaloids on Alimentary Tract: Part V. Discussion on Probable Mechanism of Constipating Action of Morphine. G. N. Myers.—p. 583.
Chemotherapy in Cerebrospinal Meningitis in the Sudan. R. M. Buchanan.—p. 605.

Lancet, London

2:443-474 (Oct. 12) 1940

- Experience at Casualty Clearing Station. J. J. M. Brown, W. M. Dennison, J. A. Ross and D. Divine.—p. 443.
*Radiography in Postoperative Ileus. P. B. Ascroft and E. Samuel.—p. 445.
Treatment of Pneumonia with Sulfapyridine and Serum. T. Anderson and J. G. Cairns.—p. 449.
*Sulfathiazole in Treatment of Pneumococcal Lobar Pneumonia. W. F. Gaisford and W. Whitelaw.—p. 451.
Toxic Manifestations of Calcium Therapy in Heart Failure. A. S. Rogen.—p. 452.

Roentgenography in Postoperative Ileus.—Ascroft and Samuel report a study of radiologic diagnosis of intestinal obstruction. Of 75 cases treated, 18 belong to the postoperative group; in most there was peritonitis, and symptoms developed of the type of ileus usually called paralytic. The plain roentgenograms were a great help in assessing individual cases. Whenever the abdomen is opened, the motility of the gastrointestinal tract and, to a lesser extent, its secretory and absorptive capacity are disturbed, producing adynamic ileus. This

condition is nearly always transient, subsiding in from six to twelve hours, and needs no special treatment; but, when there is peritonitis, especially if it is due to bacteria, adynamic ileus persists, and the abdomen may become greatly distended. All the signs of intestinal obstruction are present save one: there is no peristalsis. This makes diagnosis easy and obviates an attempt to relieve an "obstruction" by operation. The same applies to the rare instances of severe and persistent adynamic ileus uncomplicated by peritonitis. However, most cases causing anxiety after operation are not of this type. The authors show that most cases of postoperative ileus causing anxiety are due either to focal obstruction at the line of suture or, more commonly, a diffuse or peritonic obstruction. Plain roentgenograms give evidence of obstruction in both types of case. In 5 cases of suspected focal obstruction, roentgenography excluded obstruction, no operation was performed and recovery occurred. In 9 cases of peritonic obstruction, roentgenography demonstrated obstruction of the small intestine. In cases of obstruction, plain roentgenograms taken in the erect position show distention of the small bowel with fluid levels in the distended loops. In cases not requiring immediate operation intestinal drainage by suction through a duodenal or Miller-Abbott tube should be combined with serial roentgenography. Reliance on clinical signs alone may lead to dangerous delay, but roentgenography will show whether the obstruction is persisting.

Sulfathiazole in Pneumococcal Lobar Pneumonia.—Gaisford and Whitelaw employed sulfathiazole in a series of pneumococcal lobar pneumonias and sulfapyridine for alternate patients as controls. Ten patients with true lobar pneumonia were treated with sulfathiazole. There were no deaths and only 1 patient had a complication, an empyema which was drained, with recovery. Among the 9 patients who were treated with sulfapyridine there likewise were no deaths, but 1 patient developed a sterile serous effusion. Sulfathiazole acts similarly to sulfapyridine, but it produces a less prompt fall in temperature. With this temperature lag there is a correspondingly longer period of acute illness. This renders sulfapyridine the drug of choice in severe cases. The chief point in favor of sulfathiazole is that it does not cause vomiting. It is possible that a combination of sulfapyridine and sulfathiazole may come to be a valuable routine in the treatment of pneumonia, the first large doses given being sulfapyridine (e. g. the first 8 tablets) and the following ones sulfathiazole. In this way vomiting can be obviated entirely. An alternative is the use of a mixture of the two drugs from the outset, e. g. 2 tablets of sulfapyridine given with 2 tablets of sulfathiazole four-hourly for the first three doses and then one tablet of each. The first method has already been used since these investigations were undertaken with satisfactory results.

South African Medical Journal, Cape Town

14:331-350 (Sept. 14) 1940

- "Eclipse Blindness." J. S. du Toit.—p. 333.
Bilharzial Lesions of Testis. M. Gelfand and G. B. Davis.—p. 334.
Aspects of Civilian Plastic Surgery. J. Penn.—p. 335.
Intramuscular Injection of Uroselectan for Pyelograms in Infants. V. Vermooten.—p. 339.

Chinese Medical Journal, Peiping

58:141-262 (Aug.) 1940

- Osteomalacia: Clinical, Metabolic and Pathologic Studies of Case with Parathyroid Hyperplasia and Right-Sided Cardiac Hypertrophy from Thoracic Deformities and Vitamin B₁ Deficiency. S. H. Liu, K. Y. Ch'in, H. I. Chu and H. C. Pai.—p. 141.
Concentration of Sulfanilamide in Aqueous Humor of Human Eyes, with Special Reference to Local Application. T. H. Luo and S. Y. Pan.—p. 167.
Hemolytic Anemia with Erythroblastemia: Report of Three Cases Seen in Chinese Infants. C. Y. Wang and F. Y. Khoo.—p. 177.
Use of Microsedimentation Test in Tuberculous Children. C. Y. Wang.—p. 193.
Study of Aspirated Sternal Bone Marrow in Pellagra. M. S. Hwang, P. T. Kuo and W. Shih.—p. 206.
Inoculation of Monkeys with Leprosy Following Diet of Colocasia: Preliminary Report. D. R. Collier.—p. 213.
Anopheline Mosquitoes of Yunnan; Notes on Their Breeding Habits and Adult Behavior. T. L. Chung.—p. 218.
Some Epidemiologic Observations on Scarlet Fever in Peiping. K. H. Li.—p. 234.
Rat-Bite Fever in Kweiyang: Report of Two Cases. C. S. Yang.—p. 245.

Schweizerische medizinische Wochenschrift, Basel**70:873-900 (Sept. 14) 1940. Partial Index**

Sulfapyridine and Sulfathiazole in Treatment of Pneumonia. W. Löffler.—p. 873.

*Secondary Effects of Sulfapyridine. R. Heggin.—p. 881.

*Sulfathiazole Therapy in Epidemic Cerebrospinal Meningitis. W. Pulver.—p. 887.

*Single Massive Doses of Sulfathiazole in Chemotherapy of Gonorrhea. H. Miescher.—p. 891.

Sulfapyridine and Sulfathiazole in Treatment of Furuncles of Upper Lip. F. Wyss-Chodat.—p. 892.

Abdominal War Wounds. T. Naegeli.—p. 894.

Secondary Effects of Sulfapyridine.—Heggin reports the secondary effects observed in connection with the use of sulfapyridine in more than 450 cases of pneumococcal, meningococcal and gonococcal infections, with granulocytopenia (1 case, terminating fatally) and grave hematuria (5 cases) ranking as the worst effects. Nausea, vomiting, hematuria, mild anemia, cyanosis and cutaneous manifestations (3 per cent) were observed almost regularly. Latent and slowly developing granulocytopenia manifested itself suddenly in a patient with unilateral pneumonia, with high fever, though the drug had been discontinued for some time and the patient felt completely well. Renal lesions were disclosed in grave hematuria, in 1 case evolving into anuria, with increased residual nitrogen. Hematuria often presented a clinical picture of a pronounced renal colic due to calculus, an intense pain extending from one or both kidneys into the testicles and involving only a mechanical lesion, leaving the glomeruli unaffected. Copious water ingestion, regarded by the author as a necessary therapeutic adjuvant in renal stone due to the drug, released large quantities of gravel, acetylsulfapyridine forming the chief constituent. The author believes that, though grave secondary effects cannot be avoided because of the relatively high doses required for treating pneumonic infection, sulfapyridine has proved its chemotherapeutic value. However, the possibility of untoward effects should constantly be borne in mind in order that appropriate counteractive measures may be duly employed. Secondary effects of a nonserious nature, such as nausea and vomiting, may acquire so pronounced an intensity as to necessitate discontinuation of the drug and thus jeopardize the patient's chances of recovery. Granulocytopenia induced by sulfapyridine is not necessarily fatal. An erroneous diagnosis would see in the clinical picture a reactivation of the infection and resume the use of the drug, whereas, in reality, blood analysis would show that damage had been done to the bone marrow. Hematuria ought not to be lightly regarded, as it may lead to anuria. When anuria has set in, cystoscopy is urgently indicated. Sulfapyridine, though parenterally given, was found excreted in the gastric juice, in one case with a 30 per cent concentration. No injurious secondary effects were noted on the nervous system.

Sulfathiazole in Epidemic Cerebrospinal Meningitis.—Pulver found sulfathiazole effective in epidemic cerebrospinal meningitis. Of 26 patients treated solely with this drug (their age level ranged between 1 and 61 years [19 under 16 years]), all recovered save 2, thus yielding a mortality rate of 6.9 per cent compared with a 50 per cent death rate previously noted during a ten year period. Cerebrospinal fluid tests disclosed *Neisseria meningitidis* in 23 of the cases and its subsequent disappearance within three to seven days after medication. (Nasal and pharyngeal smears had detected the micro-organism in only 2 cases.) Blood tests showed in individual cases a decrease in the leukocyte count from 24,800 and 30,200 to 5,800 and 6,700 leukocytes respectively within two days. Biochemical analyses made at regular intervals disclosed a rapid return to normal levels in the sugar, total albumin and chloride content of the blood. The author's experiments in reducing dosage to the lowest quantities compatible with therapeutic effects were finally stabilized at from 12 to 20 Gm. within four to seven days, but allowing for increased dosage in complications. Initial doses in adults of from 1 to 2 Gm. and in children of from 0.1 to 0.15 Gm. per kilogram of body weight and totaling from 6 to 8 Gm. within twenty-four hours were reduced after defervescence to one third and one half of the original dosage. In the majority of cases these quantities of the drug were able to lower fever of 100.4 to 104 F. to subfebrile or normal conditions within twenty-four to forty-

eight hours. In order to prevent reactivation the drug was continued for several weeks more. Among the significant effects reported by the author is the observation that some of the children and adults brought to the clinic in a semi or total state of unconsciousness in the morning were able to play in their beds or read the newspaper in the evening. However, headache and cervical rigidity tended to linger for from two to ten days. The drug was administered intramuscularly, in exceptional cases intravenously with dextrose, and caused no local inflammation. Its superior atoxicity was seen in the absence of such secondary effects as granulocytopenia, hemolysis, hepatic lesions, renal irritation and grave cyanosis. A stubborn case of granulocytopenia in a boy aged 8 years with final recovery and a case of neuritis with metastatic acute arthritis of the knee joints are cited by the author as the only evidence of toxic damage produced by the drug. No intraspinal injection was practiced. The drug was found efficacious even in cases of seriously delayed medication.

Sulfathiazole as Chemotherapeutic Agent in Gonorrhea.—Miescher reports the cure of 14 out of 15 male patients, mostly with uncomplicated gonorrhea, by means of a single peroral dose of sulfathiazole. The massive dose, varying between four and ten tablets of the drug (tablet 0.5 Gm.), was either mixed with sugar and placed on the tongue in powdered form or dissolved in water and ingested in 0.5 liter of a native tea. No untoward effects nor relapses were observed. The single dose therapy represents an experimental evolution first from favorable results obtained by combining local and intramuscular vaccines with sulfathiazole for the cure of acute and chronic gonorrhea and then from the exclusive use of sulfathiazole spread over a progressively diminishing period of time. In these experiments the author had observed a reduction in gonococcus count and in gonorrheal discharge usually twenty-four hours, frequently also even twelve hours after medication. Single doses of ten tablets (5 Gm.) are regarded by him as approximating highest levels of tolerance.

Minerva Medica, Turin**2:217-240 (Sept. 1) 1940. Partial Index**

Eupaptic and Carminative Substances: Clinical Researches for Effects. A. Bellomo and R. Bologna.—p. 217.

*Immediate Action of Liver Extracts on Reticulocytogenic Power of Gastric Juice. G. Lami.—p. 223.

Effect of Liver Extract on Reticulocytogenic Power of Gastric Juice.—Lami studied the reticulocytogenic effect of the gastric juice of 15 normal persons and of 10 patients with pernicious anemia for an hour and a half following intravenous injection of 5 cc. of a liver extract of high potency ("Hepracton"). The gastric juice was removed during fasting and after an injection of histamine alone or preceded one hour earlier by a meal of 100 Gm. of meat. Singer biologic reaction was used to determine the reticulocytogenic power of the gastric juice. The test consists of injecting subcutaneously 3 cc. of neutralized filtrates of the gastric juice to male adult white rats in which the number of reticulocytes is determined before the test. The reticulocyte curve is followed every day for one week. The filtrates can be prepared from the mixture of three or four samples of the gastric juice withdrawn at intervals of fifteen or thirty minutes after the histamine injection following the injection of liver extract alone or preceded by a meal of meat or with the separate samples of the gastric juice. A positive reaction is manifested by an increase in the percentage of the reticulocytes in the blood of the animals and indicates the presence of the antianemic principle in the gastric juice. Failure to change on the part of the reticulocytic curve indicates a negative reaction and absence of the antianemic principle in the juice. The highest figures in the reticulocyte curve occur on the second, third or fourth day of the test, which gives a positive result in normal persons and in achylic hypochromic anemia and negative results in pernicious anemia. The positive results agree with those of the Castle test. In the cases observed by the author the reticulocytogenic power of the gastric juice of normal persons was increased after the injection of the liver extract (strong positive results of the Singer test). The increase was greater when the test included a meal of meat than when it did not. The reticulocytogenic power of the gastric juice of

patients with pernicious anemia in remission from liver therapy was greatly diminished before administration of the liver extract (weak positive results of the Singer test) and did not change after administration of the extract. The gastric juice of patients with pernicious anemia who had not had liver therapy did not possess reticulogenic power before administration of the liver extract (negative results of the Singer test) but increased after administration of the extract. The author believes that liver extract injected intravenously stimulates the absorptive capacity of the gastric wall and upper segment of the intestine for the antianemic principle and stimulates the production of the endogenous factor which results in a better use of the exogenous factor and consequent production of the anti-anemic factor. The latter, as soon as it is stored in the liver, stimulates the gastric wall and the upper segment of the intestine to further production of exogenous factor and to hemopoiesis. Liver extract injected intravenously acts through a mechanism of stimulation. It acts as substitution therapy only when the gastric wall and intestine are the seat of grave pathologic lesions.

Monatschr. für Ohrenheilkunde, Berlin

74:99-152 (March) 1940

Otorhinolaryngologic Literature of Scandinavian Authors for the Year 1938. E. Jerlang.—p. 99.

- *Vitamin Therapy in Otosclerosis. M. Baer.—p. 113.
- Speech—Psychologic Observations. K. Baldrain.—p. 118.
- Cutaneous Horn of Right Auricle: Case. H. Schnaubelt.—p. 125.
- New Instrument for Maxillary Sinus Puncture. S. Krepuska.—p. 128.

Vitamin Therapy in Otosclerosis.—Baer reports unsuccessful results in experiments undertaken to modify otosclerosis in 15 cases by means of vitamins C and B₁ and a regimen rich in these vitamins, employed for several months at a time. Subjective symptoms such as headache, vertigo, anorexia and tinnitus aurium were favorably affected and the improvement credited to vitamin B₁. The author encountered a vitamin C impairment of from 600 to 1,500 and even 2,000 mg. but does not believe in a direct connection between general vitamin C deficiency and otosclerosis. Irrespective of the vitamin C index, he fed vitamins in concentrated doses to all otosclerotic patients on the assumption that a local vitamin deficiency may well coexist with a systemic sufficiency, as is seen in parodontosis, in which the osseous changes resemble those of otosclerosis and even permanent cures seem to be effected by vitamin C. He inclines to the view that otosclerosis represents a new bone growth and hence an osteitis fibrosa, which may be hereditary in some cases. The general ineffectiveness of therapeutic measures to influence otosclerosis justifies any rational experimentation. Besides, vitamins ineffective in relation to the otosclerotic process may increase the efficacy of other medicaments employed to influence the pathologic process.

Acta Ophthalmologica, Copenhagen

18: 1-107 (No. 1) 1940

- *Malignant Exophthalmos After Strumectomy. V. A. Jensen.—p. 1.
- Demonstration of Absorption Curve of Dyestuff in Macula of Dead Macacus. E. Hanström.—p. 21.
- Nodulate Iritis (Iritis Boeck?): Three Cases. P. Kindt.—p. 38.
- Anisochromatopsia Congenita. G. W. Keyser.—p. 51.
- Rare Deformity of Upper Tear Passages in Young Girl. G. W. Keyser.—p. 55.
- A Family with Groenouw's Keratitis. H. Malling.—p. 58.
- Conjunctival Lymphoma. J. P. Jensen.—p. 67.
- Sclerodema with Ophthalmologic Changes: Case. A. Stenbeck.—p. 76.

Malignant Exophthalmos After Strumectomy.—Jensen describes four cases of exophthalmic goiter in which malignant exophthalmos developed after strumectomy. Malignant exophthalmos is characterized by a rapid and violent progression. In the beginning the patients complain only of conjunctival discomfort due to smarting pain, injection and profuse epiphora. These symptoms become manifest several months after a successful strumectomy which led to the disappearance of all hyperthyroid symptoms with the exception of ocular proptosis. Then there appear peculiar pasty thickenings of the eyelids and of the integument surrounding the eyes and pronounced chemosis with coincident aggravation of the bulbar protrusion. Violent headache develops and a painful sensation of tension across the eyes.

The protrusion of the eyeballs becomes so excessive that they are almost immobile. Enormously chemotic conjunctivas bulge out like shining red projections between the eyeballs and eyelids. Vision may become impaired as the result either of changes in the optic nerve or of the lagophthalmic keratitis, which attacks the unprotected cornea. In favorable cases in which the proptosis stops spontaneously or is checked by operation the corneal infiltrations heal, leaving leukomas, but usually they change into necrosis with perforating ulcerations and panophthalmia necessitating bilateral exenteration of the eyeballs. After removal of the eyeball the swollen orbital contents may prolapse for months through the palpebral slit, but then they undergo a gradual diminution. Malignant exophthalmos is comparatively rare. The literature contains reports of about eighty cases. Compared with the enormous number of strumectomies the rareness of malignant exophthalmos suggests that special conditions not directly concerned with the operation or the decrease of thyroid hormone make the appearance of the protrusion possible. Hyperthyroidism and proptosis may be coordinated, mutually independent phenomena. The question arises whether their common cause might be a secretory disturbance in the anterior lobe of the pituitary. This theory is supported in two different ways: (1) The adenohypophysis has a regulating influence on the function of the thyroid and (2) certain hypophysial disorders, such as Cushing's disease and acromegaly, may be attended by protrusion of the eyeballs. Experimental research suggests that malignant exophthalmos might be caused by hyperactivity of the anterior lobe of the hypophysis concurrent with a postoperative reduction in the function of the thyroid. In the beginning, corneal desiccation may be prevented by tarsorrhaphy, conjunctival plastics or bandaging with petrolatum and gutta-percha paper, but it will soon become necessary to try canthotomy and relaxing incisions in the chemotic conjunctiva and along the base of the eyelids, eventually combined with removal of orbital fat. Roentgenization of the orbit seems to be without effect. Since proptosis necessitated bilateral exenteration in many cases of malignant exophthalmos, more extensive operations have been taken into consideration. Dollinger's procedure of cutting a wedge-shaped piece of bone out of the lateral orbital wall, although successful in excessive ophthalmic goiter, has as yet not been tried in malignant exophthalmos. Naffziger suggested intracranial decompression of orbit and optic canal. With Naffziger's technic access is obtained transfrontally by two flaps of bone to the anterior cranial fossa, where the orbital roof and the upper wall of the optic canal are resected, after which the orbital fascia is opened and a relaxing incision is made in the annulus zinnii. Naffziger later extended the operation by removing also the temporal and a little of the posterior wall of the orbit. Immediately after the operation the protrusion is seen to decrease, the eyes become more mobile, the corneal ulcerations heal and the visual acuity improves. A third method suggested by Sewall and successfully applied by Kistner is the radical removal both of the frontal sinus and of the ethmoid cells. Sewall's operation supposedly is easier than Naffziger's and the resulting cicatrices are smaller. Naffziger's or Sewall's operation should be carried out as soon as the first signs of incipient optic neuritis or of corneal ulceration are observed.

Nordisk Medicin, Gothenburg

7: 1337-1372 (Aug. 10) 1940. Partial Index

Hospitalstidende

- *Essential Juvenile Anemia Due to Iron Deficiency (Chlorosis). G. Alsted.—p. 1338.
- Two Cases of Cushing's Syndrome in Men. E. W. Flensburg.—p. 1342.

Essential Juvenile Anemia Due to Iron Deficiency (Chlorosis).—Alsted describes the six cases observed in the medical department of the Frederiksberg Hospital during the last ten years. The age distribution is somewhat higher than that reported in earlier cases and menstrual disturbances seem less frequent. There were indications that the diet had been quantitatively and qualitatively deficient. The patients responded well to massive iron therapy, a rise of 1,000,000 erythrocytes occurring within a week. The author proposes the term "essential juvenile iron deficiency anemia" instead of chlorosis.

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Opportunities in the Practice of Medicine

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Medicine probably is the only field today in which a well educated graduate is sure of making a living and also of having security if he carries disability, life and old age insurance. Except for crowding in the larger cities, there is no unemployment problem for American medical graduates. Although he will not make a fortune, as large medical incomes may be a thing of the past, the average physician's income at present probably is at its highest level. According to national figures, 30 per cent of the three and one half billion annual total cost of medical care is for physicians, or \$3,800 net per physician. However, this net figure is based on many physicians who are not in practice, and the correct average net income probably is higher. "Average incomes" may be misleading. A few very large incomes do not help the physician who is not earning enough to enable him to maintain the standards of good practice. However, physicians with extremely high and low incomes are in the minority; no physician's income can be compared with those of the leading lawyers, but physicians have not found it necessary to seek other fields to eke out an existence, as is the case with some lawyers.

One of the reasons for this difference in the status of physicians and lawyers is that the ratio of the former to the population has been declining during the past century from 1:569 (including all healers) in 1850 to 1:742 in 1940.¹ Though medical students have increased during the last twenty-five years from 14,891 to 21,302 in spite of the reduction of the medical schools from ninety-six to seventy-seven, the population has expanded faster than the medical graduates.¹ Raising the educational standards of

modern physicians, the improved quality of present medical service and the increased recognition by the public of the need for better medical care also are factors in the present status of the medical profession.

The standard of a physician's living depends on his medical training, professional and business ability, energy, personality, common sense, location, hospital and other affiliations and his specialty, including general practice as a specialty. The first six of these factors are obvious, but the last three need discussion.

LOCATION

Other areas also may need medical service, but in the South the ratio of physicians to the population is 69 per cent lower than in the North (table 1). That this dearth is not primarily due to the reduction of American physicians but rather to their maldistribution is indicated by the fact that during the last thirty years the concentration of medical men in the Northern urban states decreased only 3 per cent, from a ratio of 1:609 in 1906 to 1:629 in 1936, which is still too high, while in the South the reduction was 21 per cent to 1:1,063. In some Southern counties the ratio of physicians to population is as low as 1:4,500,² although 1:1,000 is considered necessary, especially in rural communities.³ Conclusions that the medical profession is overcrowded and that the condition can be relieved by reducing the number of students entering our medical schools,⁴ though correct for New York, Boston, Philadelphia and Chicago, are invalid for the South or any other predominantly rural area. Over half of the 241 counties in the United States with inadequate medical service are in the ten Southern states.⁵ The distribution of medical services, physicians, hospitals and nurses is more impor-

Read at the dedication of the new hospital buildings of the Lynchburg General Hospital, Lynchburg, Va., May 21, 1940.

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital, with the assistance of Miss Judith Farrar, Librarian at Duke Hospital. Many of the data were abstracted from Davison, W. C.: A Survey of Medical Education in the South, address at the inauguration of Oliver C. Carmichael as Chancellor of Vanderbilt University, and a Symposium on Higher Education in the South, Nashville, Tenn., Vanderbilt University, Feb. 4, 1938.

1. Cutter, W. D., Secretary, Council on Medical Education and Hospitals: Personal communication to the author.

2. Duke Endowment, Hospital Section, Third Annual Report, 1927.

3. Final Report of the Commission on Medical Education, New York, Office of the Director of Study, 1932.

4. Bevan, A. D.: The Overcrowding of the Medical Profession, J. A. M. Coll. 11: 377-381 (Nov.) 1936. Final Report of the Commission on Medical Education.³

5. Rural Medical Service, Chicago, American Medical Association, Bureau of Medical Economics, 1937.

tant than their actual number. There is more hazard to the public and to the medical profession from scarcity of physicians in certain areas than from overcrowding in others.⁶

This uneven distribution is even worse if it is remembered that the average age of physicians

TABLE 1.—Population per Physician in 1936

State	Population (1934)	Physicians (1936)	Population per Physician
Ten Southern States			
Alabama	2,710,000	2,105	1,287
Florida	1,575,000	1,939	812
Georgia	2,911,000	2,765	1,052
Kentucky	2,657,000	2,770	959
Louisiana	2,160,000	2,135	1,014
Mississippi	2,057,000	1,515	1,358
North Carolina	3,301,000	2,570	1,284
South Carolina	1,750,000	1,335	1,311
Tennessee	2,676,000	2,939	911
Virginia	2,446,000	2,734	895
Subtotal	24,249,000	22,807	1,063
Four Northern Urban States			
Illinois	7,876,000	11,672	675
Massachusetts	4,335,000	7,263	597
New York	13,059,000	24,013	544
Pennsylvania	9,826,000	12,889	763
Subtotal	35,096,000	55,837	629
(Total U. S. A.)	118,724,606	165,163	719

in rural counties is 52 years.⁷ In Tennessee, for example, only 43 per cent of the physicians in the cities are over 50 years of age, in contrast to 77 per cent of those in the rural areas.⁸

Another disturbing condition in the rural areas is the paucity of recent graduates; 51 per cent of the young graduates located in places under 5,000 population in 1906, but only 11 per cent of the graduates of 1915 and merely 9 per cent of the class of 1920,⁹ although 48 per cent of the population live in communities under 5,000.

FACTORS RESPONSIBLE FOR SCARCITY OF PHYSICIANS IN RURAL AREAS

The three factors apparently responsible for the scarcity of physicians in the South or in any other rural area are the financial return, scattered population and living conditions.

Financial Return.—A survey⁹ of three rural counties in Tennessee, Georgia and Mississippi in 1931 demonstrated that the money spent for medical care was inadequate to remunerate practitioners or to support hospitals and other medical facilities. Three reasons tend to be responsible for this low economic status: (1) The

per capita spendable money is low, (2) a year of unfavorable weather or a lowered market for cotton, the chief "money" crop, creates a depression and (3) the Negro population decreases the economic average and increases the need for medical care. However, voluntary hospital care associations will greatly improve the situation. For example, the annual hospital bills in these three counties varied from nothing to \$319, but if spread over the population the annual cost would have been 98 cents per capita. If hospital bills can be met, the people usually can and do pay their professional charges. A recent survey of the capacity of the various states to absorb more physicians, based on their need for and ability to support medical service (table 2), ranked the ten Southern states eighteenth to thirty-ninth.

At present, owing to the improvement in farming conditions but more especially to the dearth of physicians and to the absence of competition, the incomes of the keener rural doctors often are equal to those of their urban brethren, and even better if the cost of living is considered. In some areas, subsidy by the community has been attempted, although this policy generally has been unsatisfactory.¹⁰ In recent years, the number of rural physicians increased 8 per cent without subsidies.

Scattered Population.—Although the density of the population is increasing in the Southern states, the rate has not been as rapid as in the North (table 3). Obviously the maintenance of a practice and of a hospital is more difficult in an area with fifty-three people per square mile than in one with 286. Furthermore, the distribution of physicians in the Southern states naturally follows the density of the population. The area per physician in North Carolina in 1927 ranged from 3.6 square miles in an urban

TABLE 2.—Relative Capacity of the Southern States to Absorb More Physicians *

Based on Their Need for and Ability to Support Medical Service			
State	Rank Among the 48 States and Dis- trict of Columbia	State	Rank Among the 48 States and Dis- trict of Columbia
South Carolina	18	Mississippi	28
Florida	19	Virginia	30
North Carolina	21	Kentucky	36
Alabama	22	Tennessee	38
Georgia	24	Louisiana	39

* Harris, D.: Opportunities for Medical Practice in the United States, Medical Economics 17: 42-47 (June) 1940.

county to 203.8 square miles in a rural area, with an average of 21.7 square miles per physician.² Improved roads, however, have greatly reduced the time consumed in making visits.

Living Conditions.—Rural life is all right if one likes it, but only those of us who were

6. Hyman, O. W.: Southern Medical Colleges Must Maintain Enrollment at Least at Its Present Level, J. A. M. M. Coll. 12: 301-304 (Sept.) 1937; The Number and Distribution of Physicians in the Southern States as Bearing on the Policies of Southern Medical Colleges, South. M. J. 30: 85-89 (Jan.) 1937.
7. Pusey, W. A.: The Trend in Medical and Nursing Services, J. A. M. A. 82: 1960-1964 (June 14) 1924; Medical Education and Medical Service: Further Facts and Considerations, J. A. M. A. 86: 1501-1508 (May 15) 1926.
8. Duke Endowment, Hospital Section, First Annual Report, 1925. Mayers, L., and Harrison, L. V.: The Distribution of Physicians in the United States, New York, General Education Board, 1924. Rappelye, W. C.: Discussion, Bull. A. M. M. Coll. 2: 46 (Jan.) 1927. Weiskotten, H. G.: Present Tendencies in Medical Practice, Ibid. 2: 29-47 (Jan.) 1927; Tendencies in Medical Practice: A Study of 1925 Graduates, J. A. M. M. Coll. 7: 65-85 (March) 1932.
9. Guild, C. St. C., and Falk, I. S.: Surveys of the Medical Facilities in Three Representative Southern Counties, Publication 23, Committee on the Costs of Medical Care, Chicago, University of Chicago Press, 1932.

10. Pusey, W. A.: Medical Education and Medical Service, J. A. M. A. 84: 281-285 (Jan. 24), 365-369 (Jan. 31), 437-441 (Feb. 7), 513-515 (Feb. 14), 592-595 (Feb. 25) 1925. Ordway, Thomas: A Medical School's Effort to Provide Physicians for Rural Communities, Proc. Ann. Cong. Med. Educ., 1929, pp. 28-30.

raised in the country appreciate its charm, even though the radio, movies and better roads are rapidly ameliorating the isolation and lack of amusements and are improving the living con-

TABLE 3.—Density of Population per Square Mile *

State	1910	1930
Ten Southern States	41.7	51.6
Alabama	13.7	26.8
Florida	44.4	49.5
Georgia	57.0	65.1
Kentucky	36.5	46.3
Louisiana	38.8	43.4
Mississippi	45.3	65.0
North Carolina	49.7	57.0
South Carolina	52.4	62.8
Tennessee	51.2	60.2
Virginia		
Average	43.07	52.77
Four Urban Northern States		
Illinois	100.6	136.2
Massachusetts	418.8	528.6
New York	191.2	264.2
Pennsylvania	171.0	214.8
Average	220.40	285.95

* U. S. Bureau of Foreign and Domestic Commerce: Statistical Abstract of the United States 58, Washington, D. C., Government Printing Office, 1936.

ditions. However, the social factor of unfamiliar surroundings, as well as the uncertainty of financial returns, probably deters the surplus city physicians from migrating into the country.⁶ Not only are “city raised” physicians unhappy if they locate in the country but their patients often do not like them. A few “city raised” physicians have settled from time to time in one rural county with one physician to 4,000 of the population but moved away within a year as they could not establish practices, although the “country raised” physicians in that area have more than they can do and welcomed additional practitioners.

The South will not get its physicians by migration; the students should be Southern, and to get country doctors it must be possible for students from the rural counties to study medicine. “We are oblivious to social facts in trying to devise some plan to get our graduates to go to the country. That is impossible with city graduates. Our real problem is to devise a plan whereby we can get students to come from the country. They are the ones from whom the rural practitioner must be recruited. The country lawyer, the country preacher, the country banker and business man, as the country doctor, do not go from the cities; they come from the country. And unless we succeed in devising some exotic substitute which the country will accept, we shall have to devise some plan whereby the country doctor can be developed from the country boy.”⁷ Graduates tend to return to the environment to which they are accustomed. For example, 83 per cent of the country students at the University of Tennessee returned to rural practice, and 80 per cent of the urban youths later practiced in the city. In Tennessee a campaign of publicity from 1925

to 1930 called attention to the need for country doctors. The ratio of students from rural counties at the University of Tennessee College of Medicine responded at once, and by 1927 the number of graduates going into country practice began to increase.⁶ No accurate figures are obtainable on the percentage of rural students in other medical schools compared to the ratio thirty years ago, but apparently it is much lower.

Rural students, owing to the poverty of farmers, rarely are wealthy or have resources for raising money. Probably the best way by which a sufficient number of country students can attend medical school is through loan funds, which can be repaid over a period of years and thus become available for future students. Scholarships, such as those of the Commonwealth Fund, for students who agree to practice in the country, are splendid and have demonstrated their success but require too great an outlay to be widely available and usually do not create in graduates a healthy sense of obligation toward their community and university. A revolving loan fund on which 6 per cent interest is charged is an ideal investment for university endowment funds, as medical students can and do repay their debts, and it will enable keen rural students to return to country practice. Medical schools should trust their product; if they have no confidence in them, who will? Duke students after their first year may borrow up to \$450 a year at 6 per cent,

TABLE 4.—Population per Hospital Bed in 1936

State	No. of Approved Hospitals *	Total Approved Hospital Beds	Population per Bed
Ten Southern States			
Alabama	4	1,296	2,091
Florida	3	745	2,114
Georgia	7	1,606	1,813
Kentucky	8	1,762	1,508
Louisiana	8	3,934	551
Mississippi	0	0	0
North Carolina	11	1,797	1,837
South Carolina	4	1,109	1,578
Tennessee	10	2,679	999
Virginia	7	1,512	1,586
Total	62	16,470	1,472
Four Northern Urban States			
Illinois	54	12,787	225
Massachusetts	35	9,888	438
New York	96	37,959	344
Pennsylvania	78	23,156	424
Total	263	83,790	419

* These hospitals have 50 per cent of the total bed capacity of the United States, although they represent only 10 per cent of the total number of hospitals.

and the principal is repaid in instalments starting two years after graduation. An average of \$10,000 lent annually has enabled practically every Duke medical student to continue his education. A state which needs physicians could obtain them, not only without cost, but actually at a profit by establishing similar loan funds. Cheaper medical education is not a solution.

HOSPITAL FACILITIES

The distribution of physicians and that of hospitals are mutually dependent. Physicians rarely will practice and remain in a community without hospitals, and a hospital without adequate medical personnel is not a hospital but a somewhat dangerous hotel. The young, highly trained physician of today does not feel that he can practice modern medicine without access to a hospital. Even though 90 per cent of patients can be and are properly cared for in their homes or in the physician's office,¹¹ the laboratory facilities of a hospital are essential for the diagnosis of many conditions. The establishment and maintenance of rural hospitals in North and South Carolina with the aid of the Duke Endowment not only is improving the medical service in the country but also is attracting young graduates there. In addition, local hospitals influence the older physicians who have kept abreast of the times to remain in rural communities. One of the major objectives of the Duke Endowment is to bring about a better distribution of well trained physicians by an improvement and an extension of available facilities for the practice of modern medicine which exist in and not apart from hospitals.¹²

A complete medical service is a tripod of which the three legs are (1) hospital facilities, (2) nurses and technicians and (3) physicians,¹³ the last being the basic element. Modern medicine often is unsatisfactory without modern facilities not only for the seriously sick who are brought to the hospital but also for the less seriously ill who are to be found in their homes throughout the country. The influence of the location of hospitals on the distribution of physicians is strikingly illustrated in North Carolina; in the fifty-seven counties which have hospitals there is one physician to every 1,149 people, and in the forty-three counties without hospitals the ratio is 1 to 2,034.¹⁴ Of the 638 ten year graduates who have settled in North Carolina since 1925, only sixty-four located in towns without hospitals.¹⁵

The phenomenal growth of hospitals in the United States has been reflected in the South, but the Southern hospitals still have a much smaller average number of beds, and the population per hospital bed is thrice that of the urban North (table 4).

Not only do rural communities need hospitals, but equally important, if they have a hospital, they require financial assistance to enable the people to use the hospital. Bed occupancy is as

vital as the beds themselves. Modern medical service cannot exist without hospitals, and hospitals cannot survive without support from endowments, state, county or federal aid, or voluntary hospital care associations. Because of present financial conditions, endowments are becoming rare, and state, county and federal aid may bring political control.¹⁶ The voluntary group hospital care association seems to be the logical answer. England started the movement, and Texas and North Carolina demonstrated its practicability in the South. Church gifts to hospitals help, but the hospital contributions of the 2¾ million members of one denomination have averaged less than 1.5 cents per member annually, while the Hospital Care Association in Durham, N. C., paid the hospitals an average of \$7.13 per member annually.

SPECIALTY

The answer to the question "Is the general practitioner doomed?" is "No," and that to the query "Is the profession overspecialized?" is "Yes." It is true that only 25 per cent of the recent graduates intend to do general practice,⁸ that the number of general practitioners has been steadily growing less, and that the average age of those left is increasing. However, as a well trained general practitioner can and does successfully treat over 80 per cent of disease, and as his volume enables him to treat his patients at a lower cost, the public needs and wants more general practitioners. The fact that 75 per cent of the present graduates are or plan to be specialists who are needed by less than 20 per cent of the patients is an indication not only of the overcrowding of the specialties but also of the urgent need and wide open opportunities for good general practitioners. This plethora of specialists has caused such competition and crowding that in many Southern communities the financial rewards of general practitioners, with their reduced competition, are higher than those of specialists. The modern medical curriculum often is blamed for this trend toward specialization, but the tide toward general practice is turning without any changes in the medical schools; it is a response to economic conditions.¹⁷ Since the law of supply and demand is causing a larger percentage of the present graduates to enter general practice, it behooves medical schools to study this field so that students may be better prepared for it.

An analysis of the diseases treated by Tulane graduates indicates that a general practitioner's visits consist of obstetrics and gynecology 10 per cent, minor surgery 15 per cent, and the remaining 75 per cent divided among sixty-eight common conditions. Ninety per cent of

11. Council on Medical Education and Hospitals, Report, J. A. M. A. 80:1928-1937 (June 30) 1923.

12. Duke Endowment, Hospital Section, Fourth Annual Report, 1928; Tenth Annual Report, 1934. Rankin.¹³

13. Rankin, W. S.: Hospitalization, South. M. J. 24:1113-1115 (Dec.) 1931.

14. Rankin, W. S.: The Interest of the Hospital Section of the Duke Endowment in Medical Education, Proc. Ann. Cong. Med. Educ., 1929, pp. 38-40.

15. Duke Endowment, Hospital Section, Tenth Annual Report, 1934.

16. Does Federal Subsidy Mean Federal Control? editorial, J. A. M. A. 110:132 (Jan. 8) 1938.

17. Davison, W. C.: Duke University School of Medicine, Tr. M. Soc., N. C. 74:35-39, 1927.

general practice is done outside the hospital, approximately 55 per cent in the office and 35 per cent in the home. About 75 per cent of office visits are for minor surgery, respiratory infections, general medical disorders and venereal diseases, and 90 per cent of home visits are for respiratory, general medical and contagious diseases, obstetrics and minor surgery.¹⁸

A generation ago general practitioners spent most of their time treating children. Now, with the ratio of children to the total population reduced during the past twenty years from 1:3 to 1:4, with diphtheria, whooping cough, dysentery and typhoid becoming rarities, with pneumonia and meningitis successfully treated with sulfapyridine or other drugs, with congenital syphilis reduced through the expansion of the program for treating pregnant women, with infant feeding simplified, and with the mortality in children decreased 66 per cent, most of a general practitioner's present patients are adults.¹⁹ However, the need for preventive pediatrics cannot be overemphasized; 75 per cent of the deaths among children are preventable. The distribution of a general practitioner's income also has changed. Formerly approximately 50 per cent came from obstetrics, in contrast to 30 per cent of his time,²⁰ 25 per cent from pediatrics, in contrast to 50 per cent of his time, and 25 from adult medicine, in contrast to 20 per cent of his time. A recent analysis reported 20 per cent of a general practitioner's income from obstetrics, 30 per cent from pediatrics and 50 per cent from adult medicine.²¹ The percentages of time spent in each group were similar to those of the income.

One difficulty in persuading young graduates to go into general practice is their erroneous feeling that it does not carry the same dignity as that of a specialty. Since the specialty boards were created, the students have increasingly obtained the impression that general practice is what the specialists discarded. As a matter of fact, general practice is just as much a specialty as pediatrics, and the present misunderstanding would be corrected if general practice had its own specialty board and requirements. The general practitioner needs a sound scientific background as much as if not more than a specialist, so that he may be capable under all circumstances of advising the family whether the patient needs to consult a specialist.²² A rural physician needs a more prolonged training than a city practitioner, for he must be better able to meet his problems unaided.

All graduates, and especially those desiring to enter general practice, should spend at least two years in hospital work. This is required of Duke graduates, and 80 per cent of them have spent more than this minimum. These internships preferably should be "straight" services rather than "rotating," which often provide merely a smattering of several subjects. If a graduate plans to enter general practice—a consummation much to be desired—a straight medical internship for one year, a straight pediatric internship for six months and a straight obstetric internship for six months would equip him much better than the usual rotating service. Duke Hospital has made this training possible by adding to its "straight" internships in other fields a combined obstetric-pediatric internship of one year. Three months

TABLE 5.—*Graduates of the Southern Schools of Medicine in 1936*

Medical Schools in the Ten Southern States	Number of 1936 Graduates
Alabama	0*
Georgia	33
Emory (Georgia).....	55
Louisville (Kentucky).....	89
Louisiana State University.....	43
Tulane (Louisiana).....	113
Mississippi	0*
Duke (North Carolina).....	54†
South Carolina.....	45
Tennessee	102
Vanderbilt (Tennessee).....	51
Meharry (Tennessee).....	35
Virginia, University of.....	61
Virginia, Medical College of.....	82
Total	763

* The students of the two year schools are not included, as some of them subsequently are graduated from other Southern schools, although many go to Northern schools.
† University of North Carolina and Wake Forest College also have two year schools, and the latter is starting a four year curriculum in 1941.

of this time is spent in hospital obstetrics and gynecology at Duke under Dr. Bayard Carter, three months on the Outside Obstetrics Service, Charlotte, N. C., under Dr. W. Z. Bradford, five months in hospital pediatrics at Duke and one month on infectious diseases at the Sydenham Hospital, Baltimore, under Dr. M. G. Tull. It is hoped that all state boards of licensure will recognize straight internships in any field rather than only rotating services.

SUMMARY

Even though certain factors have decreased the demand for medical personnel, e. g. the reduction of preventable diseases and the increase in telephones, hospitals and nursing, the South, in order to have adequate medical service, needs nearly twice the present number of physicians (table 1) and a threefold increase in hospital beds (table 4), especially in the rural areas. The problem is to find the former, build the latter and support both of them. The twelve Southern four year schools graduated 763 physicians in 1936 (from thirty-three to

18. Bass, C. C.: Relative Proportion of Diseases and Conditions Treated by Our Graduates in Their Practice, South. M. J. 21: 1049-1054 (Dec.) 1928. Rappelye, W. C.: Discussion, South. M. J. 21: 1053 (Dec.) 1928.
19. Time 35:49 (May 13) 1940.
20. Rowland, J. M. H.: Clinical Teaching of Obstetrics, Proc. Cong. Med. Educ., 1930; also Tr. A. Am. M. Coll.
21. Hamner, J. L., and Lackey, W. J.: A Month of General Practice, South. Med. & Surg. 101:625 (Dec.) 1939.
22. Welch, W. H.: Changing Viewpoints in Medical Education, South. M. J. 24: 1121-1124 (Dec.) 1931.

113 per school; table 5). If all of them settled in the South, and they do not, they barely would replace the losses by death among the 22,807 physicians in the ten Southern states.

The solution is threefold: improving Southern medical schools, expanding Southern hospitals and making possible the education of Southern country youths. The first is being done rapidly

by the cooperative efforts of the universities and the foundations, the second can be accomplished by voluntary hospital care associations, and the third requires the establishment of loan funds for students from rural areas so that more Southern students can obtain a medical education and become Southern rural general practitioners.

Studying Tropical Medicine in Puerto Rico

MANUEL BERGNES '41 AND JOSHUA WEINER '41

LONG ISLAND COLLEGE OF MEDICINE

BROOKLYN

Last February a notice appeared on the bulletin board at Long Island College of Medicine about an opportunity for third year students to study tropical medicine in Puerto Rico. We applied and learned of the teaching project instituted by Dr. Thomas J. Le Blanc, professor of preventive medicine at the University of Cincinnati College of Medicine, and Dr. George W. Bachman, director of the School of Tropical Medicine in San Juan, Puerto Rico. Under this plan, small groups of students had, in two previous years, spent part of the summer between the third and fourth years in San Juan engaged in brief but intensive study of tropical medicine in its natural setting. Staff members of the school and of the insular health department and various hospitals and clinics in San Juan and elsewhere cooperated in the teaching program.

We sailed, June 13, on the *S. S. Coamo*. The passengers were mostly university and preparatory students returning to their homes in Puerto Rico for the summer. We were impressed with their charm, vivacity and torrents of musical language, which were too much for our Spanish. We made many acquaintances among Puerto Rican students of dentistry, parasitology, bacteriology and medicine.

The School of Tropical Medicine is one of the outstanding architectural achievements in San Juan, patterned after the Palacio de Monterey in Salamanca, Spain. The school program consisted of one week each of study in entomology, pathology, mycology and public health and two weeks of clinical work. The first week was spent under the guidance of Dr. William Hoffman, medical zoologist, who had been in Puerto Rico fourteen years. We studied the taxonomy of mosquitoes and observed in the laboratory the eggs, larvae and adults of various species of *Anopheles*, *Culex* and *Aedes*. Then we went into the field, visiting heavily infested areas and collecting larvae and adult forms. We had the experience, quite discouraging for the novice, of dissecting mosquitoes under the microscope looking for filariae.

In the parasitology laboratory was an amazing collection of material for the study of para-

sites prevalent in Puerto Rico and elsewhere. The laboratory studies were supplemented by excursions to the haunts of the insect vectors, in the course of which we absorbed information concerning the local flora, fauna and mores.

The last day in the department of medical zoology was devoted to field work on a larger scale. We observed poorly protected cesspools and other breeding places for mosquitoes in the vicinity of human habitations and found the larvae of *Anopheles* in abundance. We searched for the molluscan host of *Schistosoma mansoni*, the fresh water snail *Australorbis glabratus*, which thrives in the contaminated waters of certain streams. As we collected snails, small boys wading in the streams were seen to have splenomegaly and ascites characteristic of schistosomiasis. This was a forceful demonstration of the presence of this disease in these river valleys.

The week end was spent traveling across the island visiting hospitals, clinics and other places. We left San Juan and drove along the old Spanish road, the Carretera Militar, through Rio Piedras, Caguas, Cayey, Aibonito, Coamo and Juana Diaz, reaching Ponce on the Caribbean coast. In Ponce we visited La Clinica Pila, Tricoche City Hospital and St. Luke's Hospital, where much clinical material was demonstrated to us. From St. Luke's, which is on a hill, could be seen the entire city and in the distance the aptly named island Caja de Muerto, which rests on the Caribbean Sea like a giant coffin. The next stop was the Ryder Memorial Hospital in Humacao, where some unusual cases of tropical disease were demonstrated.

At Santiago Island we visited what is said to be the world's only free range primate colony. Afterward we drove through the Caribbean National Forest, up to the crest of El Yunque, where the vegetation was of rare variety and interest.

The second week at the School of Tropical Medicine was devoted to the pathology of tropical disease and the special problems connected with the practice of medicine in the tropics.

Under the teaching of Dr. Enrique Koppisch, these studies were carried out in a large room in the tower, which commanded a view of the harbor, the airport, the mountains, the city and the ocean. This week was given to malaria and blackwater fever, schistosomiasis, chromoblastomycosis, the filarial diseases, elephantiasis, leprosy, madura foot and mossy foot, sprue, balantidiasis, yellow fever, yaws, ainhum and hydatid disease. The reading of necropsy protocols and references to the literature supplemented microscopic studies of diseased tissue. Dr. Koppisch presented the material with such clarity that this week proved to be the backbone of our studies in Puerto Rico.

In the study of hematology Dr. Rodriguez-Molina emphasized the anemia of sprue, which is common in Puerto Rico. The secondary anemias associated with uncinariasis, the blood changes in malaria and in schistosomiasis, and the high incidence of eosinophilia in Puerto Rico were discussed. Almost a week was spent in studying mycology. The climate of Puerto Rico is conducive to the growth of fungi. Lectures were supplemented by the study of cultures and by clinical contacts with the diseases discussed.

A week with the Department of Health impressed us with the work being carried on under the dynamic Commissioner of Health, Dr.

Garrido Morales. We saw the subsoil drainage program of malaria control, from the making of the cement pipes to their installation with subsequent conversion of malarial swamp-land into cane fields. Hookworm is being controlled by the distribution of latrines manufactured by mass production methods. Tuberculosis, a serious problem in Puerto Rico, is vigorously attacked. We visited the sanatorium at Rio Piedras, the clinics devoted to the pneumothorax treatment of ambulatory patients, venereal clinics, bacteriologic laboratories, pediatric clinics, health centers in the smaller towns, the mental hospital and the leper colony, where there were fifty-four lepers.

The clinical work consisted of ward rounds at the University Hospital of the School of Tropical Medicine, the Presbyterian Hospital and the Bayamon District Hospital, the latter the first of a number of projected 300 bed well equipped district hospitals. The ward rounds brought us to realize that, although tropical diseases may present themselves as single diagnostic entities, they more often appear in conjunction with other diseases which constitute the problems of general medicine.

We returned to El Yunque for a farewell party with those who had so hospitably received us. On August 5 we were back in New York.

Digests and Reviews

MEDICAL EDUCATION

Abstract of remarks by A. Lawrence Lowell, President of Harvard University, Boston, published in the New England Journal of Medicine, March 21, 1940.

Education in medicine is more difficult than that in any other profession because it involves the knowledge of many subjects which, apart from their relation to medicine, have no natural connection. In a medical curriculum, gross anatomy has to the beginner no obvious connection with biologic chemistry, bacteriology or pharmacology. Each involves a brute effort of memory and is largely forgotten before the time comes for its application to the practice of medicine or surgery. Whether there is an advantage in learning more facts than can be retained depends on the nature of the facts and their effect on the mind. When fresh illustrations of a thought produce familiarity with the idea and thus render it more easily reproduced, it is well. This is true of making a diagnosis or watching an operation but it is not true of striving to memorize more facts than the mind can retain; and medical knowledge has far passed that point today. Therefore the selection of basic topics ought to replace the attempt at omniscience.

There is a disadvantage in the length of medical education, and that is the late age at which

the physician is able to begin active practice. He gets through medical school and hospital not earlier than 26—far older than a man ought to be when he begins his work in life, and in most cases too near the end of the age of greatest intellectual fertility.

At the other end of his career, if he has an appointment in a hospital he loses it, as a rule, at 62; and very commonly his private practice therewith. Perhaps the age of retirement is too early or too late—too early if it means withdrawing from the community the benefit of his experience, too late if it means turning over to his juniors the bulk of the work at the hospital while retaining some supervision and a sufficient teaching clinic.

As things stand, the man with a permanent hospital appointment—out of a useful life which could last, let us say, on the average until 70—has a maximum of some thirty-six years for conducting a practice to which he has devoted, including the two premedical years, a minimum of eight years to professional training. That seems disproportionate; what is more, the length of training has been increasing and the age of hospital retirement becoming lower.

In the last half century the age of entering Harvard, and no doubt other colleges, has been reduced almost exactly one year: from 19 and

three months to 18 and three months. I should like to see it fall six months more, for I think reasonably intelligent young men are capable of excellent intellectual development at that period of life. I should much regret to have the students of our best medical schools lose the benefit of contact with other young men in a college of liberal arts, the more so because I lament the withdrawal, as compared with former times, of the physicians from civic affairs, to which they could contribute much.

One who has had a chance to see the medical school only from the faculty table may get impressions of value because he is detached from the interest of teachers in their fields. One sees that interest in the planning of the present Harvard Medical School with four separate establishments for the four chief laboratory subjects, each capable of containing an entire class, with its big lecture room unused three fourths of the time. The impression is that those who planned the school intended to exclude from anatomy and from physiology, for example, any infiltration of the other as something alien to its nature. The old conception was the attainment of medical knowledge by study of many separate fields; that of the present is correlating those fields into one great subject of medicine as a coherent whole.

Formerly the laboratory and clinical professors sat on opposite sides of the faculty table, and if an additional appointment was made to one group it was expected by the other also, that the balance might be maintained. Such an attitude is inconceivable today. The clinic makes constant use of a laboratory, and the laboratory teacher appreciates more fully that his aim is to fit men for practice.

The interest of the medical teacher in his own field as something distinct from medicine as a whole has been greatly reduced, partly at the Harvard Medical School by the general examination for graduation, which has caused both student and teacher to correlate laboratory and clinical knowledge in a striking way. It is strange that this highly effective device has been little copied in other medical schools, for people still regard examinations mainly as a test of work done, whereas their most important function is setting a standard of accomplishments.

For a nonprofessional observer to tell experts how to improve their methods would be presumptuous, but he may properly observe that the results are in some respects defective from the standpoint of the community and of the profession.

Vast improvements in medical education have been made in the last half century but there seems to have been a tendency to add the new to the old without eliminating some things no longer needed.

THE GENERAL PRACTITIONER AND MODERN MEDICINE

Abstract of an article by Dr. J. P. Simonds, professor of pathology, Northwestern University Medical School, published in the June 1940 issue of the Marquette Medical Review.

Medicine has always been interested in everything that can influence the well-being of mankind. The modern physician, especially the general practitioner, must be something of a botanist to understand an ailment so common as hay fever; something of a zoologist to appreciate the relation of parasites and disease; a physicist to comprehend the electrocardiograph, the action and defects of x-rays and radium; a chemist to grasp the underlying conditions of diabetes and exophthalmic goiter; an anatomist to know where to look for an inflamed appendix; a physiologist to distinguish between the normal activities of the body and its disordered functioning in disease; a cytologist to understand cancer; a pharmacologist to know how drugs may influence disease. He must be something of a herpetologist if he practices where poisonous snakes are abundant; a bacteriologist if he is to understand infectious diseases; a diplomat who can say just enough to be within the truth, but neither too little nor too much to do harm in an inquisitive patient; a psychologist in order to understand the whims of his patients; a moralist with high ideals of personal conduct; a humanitarian who loves his fellow men, and a good Samaritan to the suffering.

CRITERIA FOR SUCCESS IN GENERAL PRACTICE

Only the most brilliant men in medicine should go into general practice. Even low grade mediocrity often succeeds in a specialty; only the most intelligent, alert and active minds can attain real success in general practice. This is not a field into which graduates in medicine should drift just because they have not the intelligence, the ambition or the energy to enter a specialty; it should be undertaken as a matter of definite choice with a full knowledge of its requirements, its possibilities, its demands.

But the specialist has an important place in the practice of medicine. When the general practitioner has, after a complete study of a patient, arrived at a correct diagnosis, he may not have the opportunity or the time to develop the skill necessary to do a delicate and extensive operation. Then he calls in a surgeon. But he should be able to tell the surgeon all about the patient and his condition and he should know as well as or better than the surgeon what should be done for the patient. The general practitioner cannot in such instances complete his work for his patient unless he does call in a specialist. He is like the architect, who, with his wide knowledge of stone and steel, plumbing

and electric wiring, heating and ventilation, cannot bring into being the magnificent building unless he has the help of the man with the steam shovel to make the incision in the earth for the foundation and the structural steel worker to put in place the beams which bind the whole together.

THE GENERAL PRACTITIONER

Modern medicine is appalling in magnitude. Discoveries of new methods, new remedies, new active principles are made rapidly. The specialist has only an advancing margin of medical progress to keep up with, but the general practitioner must cover the entire field. By what criteria can the general practitioner determine what is of value among the unrelated tidbits of new medical knowledge published in countless contributions in medical journals? The "reviews" that form an important part of the medical literature today are not always helpful. Often they are mere catalogues of results of observations and experiments, without any attempt to assign them their position in the framework of modern medicine. For acceptance of what he reads the general practitioner will have to depend on his common sense, his intuition, a sense of fitness and his knowledge of correlative facts.

Medical knowledge exists in strata. Some has been deposited for a long time and is fully consolidated and therefore a sure foundation for practice. Other strata are in process of being laid down and are often disturbed by the ebb and flow of the tides of new discoveries. One must learn to recognize medical truth in both its filmy costume of the abstract as well as in the homely dress of the practical. Truth is discovered in a variety of ways.

Modern medicine is highly mechanized. Both patient and doctor lose much as a result of this change. Many teachers today, especially in the clinical branches, are poor examples to students of what a general practitioner should be. They have lost the self dependence and self confidence that characterized doctors of former generations. Today the physician who is the model of medical students sends his patient to the hospital, where some one in the laboratory makes an x-ray film and reports his observations, the cardiologist interprets the electrocardiogram, the pathologist diagnoses the sections of a tumor removed, a technician determines the nonprotein nitrogen of the blood and does a blood count and a urinalysis. After these experts have given the doctor the benefit of their experience in making a diagnosis, why should he do any thinking in the case? Why should he listen with utmost care to the chest and percuss the borders of the heart? The roentgenologist will tell him whether the heart is enlarged and if so whether it is a mitral or an aortic type of enlargement

or whether it is due to a cardiac aneurysm following coronary thrombosis. The roentgenologist will tell him whether there is tuberculosis, a tumor or pneumonia in the lung or fluid in the chest cavity. The intern or the resident takes the blood pressure; the nurse takes the temperature. The older doctors, using their own thoroughly trained five senses, determined most or all of these physical signs of disease themselves about as accurately as it is done today with the modern mechanical devices. And, unfortunately for both patient and doctor, the patient has to pay for all of this laboratory and x-ray work and, no matter how reasonable the doctor's fee, the patient and his family frequently feel that they have been unjustly treated.

The general practitioner, if alert, will learn how to do without many of the mechanical adjuncts of medicine. He will gain in self confidence and in self respect, he will win the respect and confidence of his patients as well as their gratitude because of his fair treatment of them financially, and he can be just as good a doctor as his more highly mechanized teachers.

OPPORTUNITY TO SAVE MEDICINE FROM SOCIALIZATION

We hear much of socialized medicine. The practice of medicine, because of its intimately personal nature, cannot be successfully regimented. Of all our citizens, the general practitioner can do more to save our threatened system of free enterprise than any other single group. When general practitioners tell their patients what the loss of our system of free enterprise will mean to them and to every one in this country, what meddling with the practice of medicine by bureaucrats will mean to the health of their children and their community, how socialization or state control of medical practice might well be a prelude to the complete destruction of free enterprise, they know that what he says is true. The general practitioner occupies not merely a strategic position in this changing world but he can, more than most groups, control the direction and extent of the change that must come with changing conditions. His quiet comments and advice, his reputation for justice and fair dealing, his common sense will do more to prevent the disasters that would follow the regimentation of medicine under the state or under any alien social order than any other one social force.

General practice is the very foundation of the science and art of medicine in this country. The work of the general practitioner is the criterion by which may be judged the quality of the medical service of any community. He is the strongest line of defense against the

invasion of medical practice by those who are untrained and unqualified either to render or to control such services. He will be a strong force in maintaining our system of free enterprise. In paraphrasing the words of Goldsmith:

*Ill fares the land, to disease and death a prey,
Where bureaucrats accumulate and doctors decay.*

FUNCTIONS OF THE PRECLINICAL SCIENCES

Abstract of an article by Dr. Magnus Ingstrup Gregeresen, professor of physiology, Columbia University College of Physicians and Surgeons, and published in Science, March 29, 1940.

The general purpose of a medical school is to train physicians. This training is constantly undergoing changes resulting from advances in science. The student must realize at the start, therefore, that he must obtain a foundation which will not crumble under these advances. He must develop a capacity to alter his concepts according to new facts and establish the habit of assimilating facts in a way that will increase his confidence even as he finds some of his earlier training misconceived. Much of what he will learn rests on insecure experimental evidence. Other phases of his work will be well founded. He must learn to distinguish between the two. This he can do only by drawing his own conclusions from what he regards as well established facts. Such a scientific attitude is the student's most valuable weapon.

A large part of the medical course is devoted to studies in which the student has no contact with patients. These studies are designed to give an understanding of the structure and function of the body. For this purpose medical schools support large faculties and expensive laboratories.

The emphasis on research in preclinical departments is criticized by those who do not fully understand the relation of these sciences to experimental medicine and to the intent of faculties of medicine in training students. The spirit of research has a vitalizing effect on the teaching staff. By stressing this experimental attitude in teaching students the preclinical sciences fulfil their most important function in medical education.

The part of the laboratory is to train the student to make his own observations, in order that these may form the groundwork on which he builds his knowledge. In many instances the technics he employs are also to be his tools

in clinical studies, and it is important that he examine them critically. Above all, the purpose is to establish confidence in his power to observe and to reason correctly from his observations. This can be accomplished only by practicing the experimental method.

A phase of teaching about which there is a difference of opinion is the writing of theses based on the reading of original articles. Scientific literature is vast. Practice in finding one's way in it, learning to get the gist of articles without great waste of time, is a necessary part of medical training. Students who depend solely on textbooks miss the flavor of scientific inquiry. The medical curriculum makes heavy demands on students. How to keep them from becoming confused and swamped is a problem that falls mainly to the lot of the preclinical departments, which they meet in their first year.

I cannot overemphasize the necessity of correlating facts from the very start of your course. Don't expect to see or be shown at once the relation of each detail to the practice of medicine. You cannot start at both ends at once. Begin with the small circle of facts under immediate observation and let the extent of your attempts to correlate grow with your acquisition of knowledge. Gradually will come general principles which will serve to simplify the learning process.

Stimulation of the student's will to learn is the chief purpose in pointing out the practical application of certain facts to medical problems. One must not devote too much time to this approach in the preclinical courses, for it may focus the student's attention on specific facts that happen to be of immediate practical value rather than on knowledge of the science as a whole. Failure to observe the difference between fact and its interpretation has caused many needless controversies. You will find that there are contradictions in the opinions and interpretations of instructors in different departments. These need not be a source of confusion, provided we agree on the facts. Some professors impress their opinions on students with such authority that these opinions are regarded as unalterable facts. We must guard against this tendency, for nothing is more destructive to the freedom of thought and creative thinking, the very qualities we aim to encourage. The student must never feel that he will be penalized for expressing an honest well founded contrary opinion in our midst.

DO YOU KNOW WHAT PHYSICIAN—

1. Wrote "The Chambered Nautilus"?
2. Was a candidate for the nomination for President of the United States in 1920?

3. Designed the United States Capitol in Washington, D. C.?

The answers are on page 2238

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items for consideration for publication in the Student Section.

Columbia Students Assisted

In the annual report for the year ending June 30, 1940, the dean of Columbia University College of Physicians and Surgeons, New York, states that during the year 115 students received scholarships and grants totaling more than \$40,000. The average award was \$354. Many of the students obtain employment during vacations, and even a larger number work throughout the school year in order to continue their studies. More than 50 per cent of the entire student body has been assisted by scholarships, loans and employment. It is to be hoped, the dean says, that more financial aid can be obtained for the students who have a class, hospital and clinic schedule which makes remunerative employment difficult, to say the least, and who face long internships and hospital training which make substantial borrowing undesirable. Scholarship aid is by all criteria the most satisfactory manner of helping many deserving young men and women ambitious to render public service through some phase of medical practice, science, teaching or health work.

Johns Hopkins Medical History Club Celebrates

The famous librarian Dr. John S. Billings in 1889 brought from the Surgeon General's Library in Washington, D. C., to a meeting in Baltimore several rare medical publications and manuscripts, an incident which stimulated interest in medical history and led to the establishment by Drs. William Osler and William Welch of the Johns Hopkins Medical History Club, which celebrated its fiftieth anniversary November 18. Osler was unflinching in his attendance at the meetings of this club, and it was on these occasions that such well known essays as "The Alabama Student," "Thomas Dover," "John Keats, the Apothecary Poet" were presented before the students and others in attendance.

Jobs for College Students

More than 150,000 young people are being enabled to continue their education in the nation's colleges and universities during the present academic year through jobs provided under the college and graduate work program of the National Youth Administration of the Federal Security agency, it has been announced. Colleges and universities have been assigned employment and fund quotas on the basis of 9.47 per cent of the total number of resident undergraduate and graduate day students from 16 to 24 years of age, enrolled as of Nov. 1, 1939, and carrying at least three fourths of a normal schedule. For the academic year 1940-1941, the national student quota is 101,846. Figures compiled as of April 1940 show that the National Youth Administration paid an average monthly wage of \$13.46 to college and graduate students participating in the program. The average wage of the undergraduate was \$13.25 a month, while that of the graduate student was \$21.78. Undergraduate college students are permitted to earn an amount, established by local authorities, between a minimum of \$10 a month and a maximum of \$20, while graduate students may earn from a minimum of \$10 to a maximum of \$30.

The total allotment of college and graduate work funds for the academic year 1940-1941 amounts to \$13,713,225. The allotments to the states are made on a monthly basis, usually over a nine month period;

however, in some instances the institutions operate on an eight month basis and are allotted funds accordingly.

Young people between the ages of 16 and 24, inclusive, who need assistance in order to continue their education are eligible for employment on the NYA college and graduate work program, which operates in nonprofit-making, tax-exempt, bona fide educational institutions. Officials of each institution have the responsibility for selecting the students and for supervising their work, which includes research and laboratory work, building and repair of equipment, construction and repair of buildings and other school facilities, clerical and stenographic work and library assistance. A total of 1,712 institutions participate in the college and graduate work program.

Hospital Residents Present Programs

Residents of St. Louis hospitals were invited to present the program before the St. Louis Medical Society, November 12. Participating from Barnes Hospital were Drs. William R. Arrowsmith and Samuel P. Harbison, speaking on "Reasons for the Failure of Iron Therapy in Certain Cases" and "Crystalline Sulfanilamide and Wound Healing" respectively; from City Hospital, Dr. Leo V. Mulligan, "Major Amputations in Gangrene of the Lower Extremities," and from Firmin Desloge Hospital, Drs. Henry E. Oppenheimer and Joshua E. Jensen, "Observations on the Effect of Vitamin K" and "Thrombocytopenic Purpura—Relieved by Splenectomy—Report of a Case" respectively.

West Virginia Seminars

At the regular seminar at West Virginia University School of Medicine, Morgantown, November 12, the student body was addressed by Dr. William L. Mullins, assistant professor of medicine, University of Pittsburgh School of Medicine, on heart disease; in the seminar October 25, by Dr. Edward G. McGavran, county health officer, on functions of county health departments as they relate to the practice of medicine, and at that on October 11, by Dr. George R. Maxwell, Morgantown, on the heart in the practice of medicine.

Harvard Class Plans Gift to School

The class of 1925 of Harvard Medical School, Boston, at its reunion in New York in June enthusiastically approved the proposal that the class raise \$10,000 to be given to the medical school at the class reunion to be held in 1950, the money to be invested by the university and the income to be used for the medical school.

Applicants for Admission to Columbia

The dean of Columbia University College of Physicians and Surgeons, New York, Dr. Willard C. Rappleye, in his annual report for the year ending June 30, 1940, states that 413 students were enrolled in the regular course for the degree of doctor of medicine during the year, of whom 103 were seniors and 107 freshmen. There were 1,048 applicants for admission to the first year class. The students had prepared in 163 different colleges and universities. The class admitted during the year had prepared in forty-seven colleges. The graduating class obtained internships

in fifty-three different hospitals in all sections of the country. One hundred and ten students who were registered under the graduate faculties of the university took their work at the medical school during the year. Instruction in the medical sciences for the school of dental and oral surgery was provided for the students of that school. There were 194 residents in the hospitals affiliated with the graduate medical program, of whom fifty-two were registered for the degree of doctor of medical science. In the post-graduate courses offered at thirteen hospitals, 1,061 physicians were registered from forty-three states and twenty-three foreign countries.

Dr. Gates Addressed California Seniors

Senior students at the University of California Medical School, San Francisco, the faculty and guests were addressed in November by R. Ruggles Gates, Ph.D., LL.D., professor of botany, King's College, University of London, London, England, on "The Biology of Human Blood Groups." Dr. Gates in 1915 lectured at the Genetics Congress in San Francisco and in that year published his book, "The Mutation Factor in Evolution"; in 1916 and 1917 he was acting professor of zoology at the University of California. In 1929 he published a reference book on heredity in man and became deeply interested in human blood groups, which during his extensive travels he investigated in various native peoples in South America, India and Canada.

Tufts Scientific Forum

The Scientific Forum at Tufts College Medical School, Boston, is an organization that gives students an opportunity to present papers. The following students presented papers before this group during recent weeks: Alfred G. Chandler '42 on "Diagnosis of Brain Tumors"; Robert W. Riemer '42, "Nervous Indigestion"; Jerome C. Saltz '42, "Specific Treatment of Chronic Arthritis," and Dudley B. Tyson '42, "Psychoneuroses as Seen in General Practice." The president of the Scientific Forum this year is Robert W. Riemer.

Field Day at Wisconsin

To promote fellowship and better understanding between the teachers and students at the University of Wisconsin Medical School, Madison, is the object of the annual field day which is held in the spring. The day begins with a review of research being carried on by students. There are special exhibits, a luncheon, then an address by some well known guest. The respective classes give vent to their rivalries in base ball games in the afternoon and finish the day at a banquet which both faculty and students attend.

Music Room for Harvard Students

A music room has been fitted out in the students' dormitory, Vanderbilt Hall, at Harvard Medical School, Boston, for the comfort and entertainment of students, and the library has been redecorated with new lights and new chairs. The dining room rates have been changed, so that more students may be able to take their meals there.

California Lecture

The senior students and faculty of the University of California Medical School, San Francisco, were recently addressed by Wendell L. Stanley, Ph.D., of the Rockefeller Institute for Medical Research, N. Y., on the subject of viruses. Dr. Stanley during this semester is Hitchcock Lecturer at the University of California.

Duke Premedical Student Wins Scholarship

Joseph W. Taylor Jr., Tampa, Fla., a premedical student at Duke University School of Medicine, Durham, N. C., has been awarded a tuition scholarship at Duke as one of five members of his class having the highest averages. According to the *Tampa Tribune*, Mr. Taylor is also a member of Phi Beta Kappa and of other honorary clubs and a member of the Duke University golf team.

Tennessee's Comprehensive Examinations

When a student at the University of Tennessee College of Medicine, Memphis, completes the first six quarters of the medical course, the privilege of registration in the seventh quarter is withheld for one quarter until the student is given a comprehensive examination on the preclinical courses by a committee appointed from the clinical staff. The object is to determine the student's fitness to undertake the clinical courses. The examinations, which require three nights to complete, are individual and oral. The winter comprehensive examinations at the University of Tennessee College of Medicine will be held Jan. 2-4, 1941.

"DO YOU KNOW WHAT PHYSICIAN"

Following are answers to the questions appearing on page 2236:

1. Oliver Wendell Holmes, who for thirty-five years was professor of anatomy and physiology at Harvard. In 1843, while still a medical practitioner in Boston, Holmes reported his discovery of the contagiousness of puerperal infection. These observations were confirmed several years later by a young Hungarian physician, Ignaz P. Semmelweis.

2. General Leonard Wood, who graduated from Harvard Medical School in 1884 and for many years served in the medical corps of the U. S. Army. Later he was transferred to the line and became chief of staff of the army and governor general of the Philippine Islands. General Wood died in Boston in 1927.

3. Dr. William Thornton. In October 1792, Dr. Thornton requested from the commissioners an opportunity to present a plan; his request was granted and his plan accepted by the commissioners April 5, 1793. Some fourteen plans for a capitol building had been submitted by others previously, but none was wholly satisfactory. In the development of Dr. Thornton's plans in the erection of the first unit of the Capitol Building, three architects were employed—Stephen H. Hallett, George Hadfield and James Hoban, the architect of the White House. The erection of the south section of the Capitol, which is now occupied by Statuary Hall, was under the charge of B. H. Latrobe. The dome of the original central building, constructed of wood covered with copper, was replaced in 1856 by the present structure of cast iron, completed in 1865. The dome receives light through 108 windows. Dr. Thornton was born in 1761 on the Island of Tortola, West Indies, and received his M.D. degree in Edinburgh in 1784. He continued medical study in Paris and then came to Washington, D. C. He served as the commissioner of the District of Columbia for eight years. President Jefferson appointed him clerk of patents, and later he became the first commissioner of patents. Dr. Thornton became a member of the Medical Society of the District of Columbia in 1819, the year in which the society received its first charter from Congress, and was vice president of the society 1820-1823. He died, March 28, 1828 and was buried in the Congressional Cemetery.

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ROENTGEN THERAPY FOR BRONCHIOGENIC CARCINOMA

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AND

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In this review we propose to compare the results obtained from roentgen therapy in a group of 125 cases of proved primary bronchiogenic carcinoma with another group of 125 proved cases in which neither roentgen therapy nor any other form of therapy was employed. Considered here, a proved case will be regarded as one in which tissue from the tumor on microscopic examination has shown the presence of carcinoma.

In all cases in our study there was microscopic confirmation of the clinical diagnosis. This point is important, because we know from experience that to make a differential diagnosis between primary carcinoma of the bronchus and other types of pulmonary lesions is often difficult. Although roentgenologic examination of the thorax is of the utmost importance in the diagnosis of this condition, it is well known that considerable inaccuracy exists in precise differentiation between primary carcinoma and other lesions by this method.

All of the 250 patients to be considered in this study were examined by the same group of clinicians and roentgenologists, and the treatment was given by the same group of radiologists. Of course, many more patients than 125 have received roentgen therapy for primary carcinoma of the bronchus, but since there were only 125 patients who did not receive any roentgen therapy it was thought advisable in our study for purposes of comparison to limit the group who did receive such therapy to the same number as those who did not.

We were first desirous of determining whether or not there was any criterion which guided the clinician in his decision as to which patient should receive roentgen therapy and which should not. In general, the untreated patients were in more precarious physical condition than those for whom roentgen therapy was advised. However, it must be said that in the earlier days of our experience with primary carcinoma of the bronchus it was generally thought that roentgen therapy was of practically no value for this condition; consequently patients were dismissed once a positive diag-

nosis had been established, regardless of their actual physical condition.

All authorities agree that primary carcinoma of the bronchus occurs more frequently in men than in women. In our group, for every woman affected there were four men (table 1). Healthy adults in the prime of life are most often afflicted (table 2). Extremes of age may also be encountered in rare instances; one of our patients was 2½ years of age and another 80 years of age.

Many hypotheses have been advanced to account for the apparent increase in incidence of bronchiogenic carcinoma. The roles of infection, irritation and heredity all have been advocated and denied by most observers. The patients in our group were predominantly farmers, but we could not elicit any tangible etiologic factor.

Primary carcinoma of the bronchus is usually insidious in its onset, and it is often difficult to distinguish it from other forms of pulmonary disease. It may therefore be overlooked, owing to the fact that the symptoms at the onset may blend imperceptibly with the clinical symptoms that may exist as a result of other pulmonary disease. In certain instances, however, there is a history that the patient apparently enjoyed perfect health and then suffered a sudden onset of symptoms such as pulmonary hemorrhage or severe paroxysms of cough. As may be readily seen by a review of table 3, most of our patients had symptoms that dated back for several months before the patients came for examination. Nine patients gave a history of symptoms that covered a period of two years or more before a correct diagnosis was established.

From the standpoint of symptomatology there was no difference whatever so far as the clinical course was concerned between the two groups in our series (table 4). It is important to emphasize that at times primary carcinoma of the bronchus may remain silent and the presenting symptoms may be those caused by metastatic focus. It is also important to point out that negative results on roentgenologic examination of the thorax do not always rule out the possibility of an underlying carcinoma. A physical finding that should always cause one to suspect the possibility of the existence of a bronchiogenic carcinoma is the absence or diminution of breath sounds over any portion of the lung. In a number of our cases this physical finding alone led to bronchoscopic examination, with subsequent establishment of the correct diagnosis.

The sites of metastatic foci in our cases as shown by clinical or roentgenologic examination are given in table 5. It should be mentioned in this connection

From the Section on Therapeutic Radiology (Dr. Leddy) and the Division of Medicine (Dr. Moersch), the Mayo Clinic.
Read before the Section on Radiology at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

that the incidence of these signs is at variance with that given in other reports because the incidence herein given occurred among living patients.

The sites of occurrence of the bronchiogenic tumors in our cases are given in table 6. It is noteworthy that there was a rather low incidence of peripheral

TABLE 1.—Distribution According to Sex

Sex	Treatment Given	Treatment Not Given
Male.....	97	106
Female.....	28	19

TABLE 2.—Distribution According to Age

Age, Years	Treatment Given	Treatment Not Given
Less than 20.....	1	1
21 to 30.....	5	7
31 to 40.....	13	11
41 to 50.....	34	30
51 to 60.....	45	47
61 to 70.....	25	28
More than 71.....	2	1

tumors, such as those originating near the pleura, and those of the "Pancoast" type. This may be attributable in part to the fact that in the majority of the cases in our study the diagnosis was based on microscopic examination of tissue obtained through the bronchoscope. Thus, many cases in which the lesion was situated in the periphery of the lung and in which the diagnosis was not established until necropsy were not included in this study.

Table 7 illustrates the histologic classification of the tumors in our study. To avoid all controversy over classification we have divided them according to their obvious structure, that is, adenomatous or epitheliomatous, and have subdivided them according to their index of malignancy as determined by Broders personally. Such a classification is simple, clear, not ambiguous, and easy to use; it seems to us more advantageous than other more elaborate and perhaps more confusing classifications.

Outstanding in table 7 is the high incidence of tumors of the highest grades of malignancy. In fact, of the 250 tumors that we are considering, 212 were

TABLE 3.—Duration of Symptoms Before Registration

Duration	Treatment Given	Treatment Not Given
1 to 2 months.....	19	23
3 to 5 months.....	38	33
6 to 11 months.....	46	39
1 year.....	11	10
13 to 18 months.....	6	6
2 years.....	2	3
2½ years.....	1	..
3 years.....	2	..
5 years.....	..	1

of the most malignant type. There is, however, nothing remarkably different in regard to the distribution of tumors according to their index of malignancy whether in the treated or the untreated groups. As a matter of fact, the index of malignancy played no role whatever in deciding whether a given tumor was or was not suitable for roentgen therapy.

For the purpose of record it can be stated that there was one case of hemangio-endothelioma of the trachea.

One of the eight cases of adenocarcinoma grade 1 occurred in the trachea, one in the left upper lobe and two each in the right main bronchus, the right middle lobe and the right lower lobe, respectively. As is well known, these tumors are the so-called adenomas of the bronchi about which there has been much controversy.

Considering the types of patients that we have treated with roentgen rays, it is unfair to compare the value of operative procedures with the value of roentgen therapy in cases of bronchiogenic carcinoma. Even though the indications for pneumonectomy are not always followed rigidly, the radical operation is generally reserved for patients who have a relatively small localized tumor and who present no evidence of distant metastasis or of marked physical deterioration. The indications for roentgen therapy, on the other hand, are in general that the patient is not suitable for radical operation or that he refuses it. In short, operation is generally attempted in only carefully selected cases.

In the evaluation of surgical results in a carefully selected group of suitable cases, one must not forget

TABLE 4.—Symptoms and Signs

Symptoms	Treatment Given	Treatment Not Given
Cough.....	125	119
Dyspnea.....	60	76
Hemoptysis.....	51	53
Loss of weight.....	20	42
Effusion.....	28	24
Hoarseness.....	8	11
Dysphagia.....	8	8
Cyanosis.....	0	4
Pain.....	50	56
Fever.....	23	23
Clubbed fingers.....	0	3
Neurologic alone.....	0	6
Neurologic with cough.....	0	2
Edema of face.....	1	3
Strangling.....	8	8
Abdominal.....	1	0

the immediate mortality of the operation, which is still high even in the hands of the most skilled operators. To be fair, however, one must admit that progress is being made in this field and that, theoretically, radical operation still offers the patient his best chance of a cure if he survives the operation. But the patient with a bronchiogenic carcinoma is in difficult straits to decide whether to assume the high surgical risk, with a chance of curing his condition, or to take roentgen therapy, with a chance of prolonging life for an indefinite period.

On the other hand, if one abandons the idea of cure as the criterion by which the value of any therapeutic method is to be judged one can allocate to roentgen therapy a place among the valuable palliative procedures, comparable perhaps to the surgical treatment of gastric or renal cancer or to the medical treatment of cardiac, hepatic and other well known degenerative diseases. Considered thus, it seems more sensible to judge the results of roentgen therapy for bronchiogenic carcinoma from the point of view of its benefit to the patient after due consideration of the expense and the wear and tear, if not the actual misery, undergone by the patient during his treatment.

In an attempt to evaluate roentgen therapy for bronchiogenic carcinoma we will present an analysis of the results which we have obtained in a group of

125 proved cases of bronchiogenic carcinoma in which treatment has been given by various roentgenologic methods (tables 8 and 9). The terms which we have employed to designate the various kinds of treatment in the tables are sufficiently well known by most radiologists to obviate further elaboration of them. However, we should like to call attention to a point of view long held by many radiologists besides ourselves, namely that less than three courses of treatment with the "massive" technic are insufficient for all but the exceptional case. Judged in this light we think that 102 of our 125 patients had entirely insufficient roentgen therapy.

There are several reasons for this state of affairs. First, many of these patients were treated in the early days when the value of roentgen therapy was regarded as hardly greater than that of any other experimental procedure. Second, the physical condition of many patients was not good enough to justify anything more than a mild, or at most a single, course of treatment. Third, the results of the first course of treatment were

than a year after proof of his diagnosis. Such a situation shows the fallacy of a statistical analysis for "cures" and seems to indicate a fertile field in which earlier diagnosis may improve the final results.

An analysis of the results of roentgen therapy shows some interesting and, at times, paradoxical results. It

TABLE 7.—*Histologic Diagnosis*

Type of Lesion	Grade of Lesion	Treatment Given	Treatment Not Given
Squamous cell epithelioma.....	1	0	0
	2	1	4
	3	24	23
	4	39	30
Adenocarcinoma.....	1	5	3
	2	8	3
	3	18	19
	4	29	30
Effusion.....		1	12
Hemangio-endothelioma.....		0	1

TABLE 5.—*Sites of Metastasis*

Site	Treatment Given	Treatment Not Given
Other lung.....	1	3
Supraclavicular node.....	22	18
Liver.....	0	5
Central nervous system.....	3	12
Bone.....	3	4
Skin.....	1	0
Axilla.....	1	0

TABLE 6.—*Site of Tumor*

Site	Treatment Given	Treatment Not Given
Right main bronchus.....	23	26
Left main bronchus.....	12	21
Right upper lobe bronchus.....	23	20
Left upper lobe bronchus.....	14	8
Right middle lobe bronchus.....	5	3
Right lower lobe bronchus.....	31	29
Left lower lobe bronchus.....	14	15
Trachea.....	3	3

often too discouraging or too indefinite to warrant continuation of roentgen therapy. Fourth, the inconvenience of further treatment at the clinic owing to personal circumstances of the patient made complete treatment impossible. Fifth, there are no exact indications to be followed in either planning or administering roentgen therapy. Sixth, knowledge of the advantages of repeated courses of treatment, based on experience, was slowly acquired.

One of the important reasons why the results of roentgen therapy are not better is the poor general condition of the patients which precludes adequate treatment. That statement is proved by the high death rate that occurs within six months or less in both the treated and the untreated groups. Not only were ninety-nine patients in the terminal stages of the disease, but also of those who did receive some treatment little was accomplished because thirty-seven of them died within four months.

Three patients lived a year or more without treatment after histologic proof of the diagnosis. As a matter of fact, all three of these patients had roentgen therapy elsewhere, but we have listed them as untreated because they did not receive treatment at the clinic. At any rate, we do not know of a single patient who is known not to have had any roentgen therapy who lived more

does not seem that the results of technically superior treatment were consistently better. The discrepancy can be explained easily by the fact which we have mentioned before, that we are not considering all the patients who had roentgen therapy.

Twelve patients had incomplete or "placebo" treatment, and two others had roentgen therapy of moderate voltage. Rather than send these patients home untreated and in a hopeless condition, this kind of treatment was given. Not one of these patients survived for six months. All fourteen patients, who for all practical purposes were untreated, followed the course of the untreated patients.

It should be noted that the data which we are considering do not permit any conclusions regarding the merits of any technic of treatment, because not all patients who had roentgen therapy are considered herein. It so happens that most of the patients in this review were treated by the so-called massive dose technic. However, a few patients treated by the "Coutard method" are also included. We think, therefore, that the question of the best method of

TABLE 8.—*Types of Therapy Employed*

Treatment *	Cases
Placebo or incomplete first course.....	12
"Moderate" voltage.....	2
"Massive dosage" (200 kv.)	
1 course.....	66
2 courses.....	21
3 courses.....	5
More than 3 courses.....	4
(1 four courses, 1 seven courses)	
"Fractional"	
1 course (8 patients).....	10
2 courses (1 patient).....	
3 courses (1 patient).....	
"Protracted fractional".....	4
All three types.....	1

* Complete or sufficient treatment in twenty-three cases.

treatment had better remain unanswered for the present.

We have already given our reasons for not considering fourteen cases in the group when forming a judgment of the results of roentgen therapy for bronchiogenic carcinoma. If, now, we deduct those additional patients who, according to accepted criteria, were insufficiently treated (since they all received less

than three courses of treatment) there remain twenty-three patients who may be regarded as completely or sufficiently treated. The remaining eighty-eight patients had various degrees of incomplete treatment.

Regardless of the amount of roentgen therapy which they actually received, twenty-five of these 125 patients

that these results were produced by methods of treatment that have no associated mortality and also that all of the 125 treated patients were beyond hope of benefit from operation. Since no patient who was not treated with roentgen rays survived for longer than a year, and since twenty-five patients who were treated lived from one to twelve years, the absolute value of roentgen therapy as a palliative measure for bronchiogenic carcinoma seems self evident.

TABLE 9.—*Technic of Roentgen Therapy*

Treatment	Factors	Field
Placebo		
"Moderate"	135 kilovolts 5 milliamperes 40 cm. TSD 6 mm. aluminum 28 minutes = 560 roentgens	1 field, anterior mediastinum 1 field, posterior mediastinum
"Massive"	200 kilovolts 20 milliamperes 50 cm. TSD 3/4 mm. cu. + 1 mm. aluminum 20 minutes = 560 roentgens	2 fields, anterior thoracic 2 fields, posterior thoracic, in cross fire
Fractional	Same as "massive" with fewer minutes per treatment, but with same total dose	Same as "massive"
Protracted fractional	200 kilovolts 20 milliamperes 50 cm. TSD Thoreaus filter 150 to 200 roentgens for a total dose of 2,000 to 3,000 roentgens per field	4 to 6 fields

lived for at least one year after treatment. Table 10 shows the data concerning these patients. It seems to indicate that, in general, adenocarcinoma grade 1 has the most favorable prognosis of all these lesions and that, as a whole, patients with adenocarcinoma do better than those with epithelioma. Fifteen of these twenty-five patients had adenocarcinoma. Of these

TABLE 10.—*Data on Twenty-Five Patients Who Lived One Year or More After Treatment*

Lesion			Patient		Duration of Symptoms Before Treatment, Months	Course of Treatment	Survival After Treatment, Months
Type	Grade	Site	Age, Years	Sex			
A	4	RLL	41	♀	16	1	146
A	2	RM	56	♂	9	1	127
A	1	RLL	30	♂	24	2	119
A	3	RLL	30	♂	4	7	64
A	3	RM	63	♂	16	1	63
A	1	RM	25	♂	8	1	50
A	3	RUL	57	♀	6	2	31
A	1	Trachea	32	♀	36	3	33
S	4	RLL	64	♂	6	1	33
A	4	RLL	64	♂	2	2	31
A	1	RM	42	♀	3	3	29
A	4	RUL	48	♂	10	4	23
S	4	RLL	54	♀	7	1	22
S	4	RLL	54	♂	11	1	21
S	3	RLL	32	♂	5	2	18
A	2	LUL	48	♀	3	2	17
S	3	RUL	41	♂	6	1	17
A	3	LLL	62	♂	9	1	16
S	2	LM	59	♂	3	1	15
S	4	RLL	51	♂	4	4	14
S	3	RUL	38	♂	2	3	13
A	4	RLL	57	♂	36	1	12
A	4	LM	19	♀	8	3	12
S	4	RUL	44	♂	6	1	12
S	3	RUL	57	♂	18	1	12

Key: A = adenocarcinoma; S = squamous cell epithelioma; RLL = right lower lobe bronchus; RM = right main bronchus; RUL = right upper lobe bronchus; LUL = left upper lobe bronchus; LLL = left lower lobe bronchus; LM = left main bronchus.

fifteen lesions four were grade 1, two were grade 2, four were grade 3 and five were grade 4. Ten of these twenty-five patients had squamous cell epithelioma. Of these ten lesions, five were grade 3 and five were grade 4.

In evaluating our results of roentgen therapy in cases of bronchiogenic carcinoma, one should keep in mind

SUMMARY

In this series of 250 cases of proved bronchiogenic carcinoma the prognosis was poor because of the advanced stage of the disease at which a correct diagnosis was made. Nevertheless our results show not only that roentgen therapy is an excellent method of palliation but also that it has produced so-called cures. We therefore think that any patient who is not in too precarious a physical condition deserves to have at least one course of roentgen therapy; otherwise his life expectancy is, at most, one year. On the other hand, twenty-five patients in our series have lived from one to twelve years after roentgen therapy. The data are inconclusive but it seems that, in general, adenocarcinoma is a more favorable type of tumor than epithelioma. The question of the best method of treating bronchiogenic carcinoma with roentgen rays had better remain unanswered for the present.

ABSTRACT OF DISCUSSION

DR. MAURICE LENZ, New York: It is generally admitted that roentgen therapy of bronchiogenic carcinoma may relieve cough, expectoration, hemoptysis and pain in the chest. It is doubtful whether this treatment prolongs life. As it is difficult to fix the date of onset of the disease, a claim of increased survival following roentgen therapy must be based on a comparison of a sufficient number of treated and untreated patients. This has been done in a thorough and unbiased analysis of 125 treated and 125 untreated patients with cancer of the lung by Drs. Leddy and Moersch. While the results are encouraging, they naturally do not compare with the results in microscopically similar tumors in more accessible locations. The authors have emphasized the fact that patients referred for roentgen therapy of bronchiogenic carcinoma usually have extensive local disease. Vigorous irradiation is not practical in such cases because of concomitant injury to large volumes of normal lung tissue which have to be included. Added to this difficulty is the danger of increased breaking down if an abscess cavity is associated with the cancer, especially if it is situated, as is frequently the case, in an atelectatic lobe. The dosage administered in bronchiogenic carcinoma is therefore much less than that proved adequate in similar carcinomas in more accessible locations. If cases were referred earlier so that only small fields would be needed to include the entire disease, larger doses could be administered and perhaps would offer more hope. I believe that the entire dose should be administered in the first and only course of treatment before retrogressive changes in the normal tissues, due to preceding irradiation, preclude the administration of adequate x-ray dosage. On the basis of autopsy and clinical records of 121 untreated and sixty-eight treated cancers of the lung, Dr. William Tenzel, my associate at Montefiore Hospital, concluded that there was a direct relationship between the length of survival and the x-ray dose estimated to reach the tumor. Thus the length of survival was raised from eleven and a half months to twenty-two months when the "estimated tumor dose" was increased from 2,000 roentgens to about 6,000. It is only by such carefully substantiated studies as set forth by Drs. Leddy and Moersch that we may hope to convince the clinician of the importance of sending earlier cases of carcinoma of the lung for roentgen therapy, and this offers the only hope for improvement in therapeutic results.

IMPROVED TECHNIC FOR REMOVAL
OF SEMILUNAR CARTILAGE AND
POSTOPERATIVE TREATMENT

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Fifteen years ago I was impressed with difficulties attendant on internal derangements of the knee. Principles of diagnosis were not as clearly defined as at present. Operation often resulted in many weeks or several months of disability and too often produced a joint lacking full free motion. Convalescence was frequently long and painful and the entire procedure costly. In 1927 I¹ began aspirating joints and injecting air before and after operation as a matter of routine. This experience indicated hemorrhage as probably the greatest disturbing factor. Much blood in the joint before or after operation may result in irritation, infiltration, swelling and thickening of the synovial membrane and ballooning of the joint capsule. Formation of fibrin and its absorption or organization often results in adhesions within the joint. This train of events prolongs immobility. Hence a study was undertaken with a view to keeping free blood out of the joint cavity after operation.

Arthrotomy of a normal joint can be done with a minimum of trauma, with complete hemostasis, permitting early function, a minimum period of convalescence and early return to normal activity.

PREPARATION

Problems of diagnosis will not be considered except to note that, whenever increased fluid or hydrops is present, aspiration followed by injection of air to produce moderate tension within the joint is carried out. Adequate x-ray examinations are made from whatever angle may be indicated.

The state of the joint from the standpoint of arthritis is noted. A general investigation is next carried out. Possible focal infections are searched for. Occasionally I insist that an abscessed tooth be removed or prophylaxis of the mouth performed, a sinus irrigated or a pair of tonsils removed, or a chronically infected prostate or cervix first treated.

Next a careful history is taken of wound healing, whether or not ordinary scratches or cuts heal by first intention or are prone to fester. In the latter event a patient is checked with Burky's² toxin for sensitivity to staphylococcus toxins and, if necessary, a course of intradermal injections of Burky's toxin is given to raise immunity.

Careful blood studies are next carried out with special reference to the cell and platelet counts, bleeding time, clotting time, clot retraction time and the prothrombin time. If there is deviation from normal in any of these, a thorough study is carried out to determine its nature, cause and correction, particularly if there is disturbance in the clotting mechanism.

Allergy to iodine, procaine hydrochloride, narcotics or the ordinary drugs which might be used is investigated.

The knee, thigh and calf are invariably scrubbed with green soap and gauze, bristle brushes being avoided; the extremity is then shaved and the area cleaned with alcohol, ether and third-strength iodine (preferably the night before operation) and swathed in sterile towels, which are removed before operation, when the skin is coated with full-strength iodine unless the patient is sensitive to it. In these rather rare cases the gentian violet solution which I introduced³ is used.

ANESTHESIA

Local anesthesia is preferred; 3 grains (0.2 Gm.) of pentobarbital sodium is administered by mouth to adults a half hour before operation. One per cent procaine hydrochloride is used; from 20 to 40 cc. is injected into the joint after aspiration. The line of incision is next infiltrated, not more than one drop of epinephrine per ounce of solution being employed to prolong the anesthesia; a greater quantity will cause postoperative hemorrhage. Spinal anesthesia is occasionally used and rarely a general anesthesia. The more explosive types are avoided, as is the closed ether method. This precaution is necessary when the electrocautery is used.

OPERATION

The affected extremity is draped free and so arranged that it can be flexed to right angles over the side or the end of the table.

A tourniquet is never used. I agree with Aleman and Friberg⁴ that it is apt to cause thrombosis in the older patients; it increases the postoperative pain, swelling and local disturbance. A tourniquet prevents hemostasis and permits postoperative intra-articular hemorrhage. Voyer⁵ cautions against it for these reasons and believes that it lowers natural resistance to infection.

A short longitudinal or slightly oblique parapatellar incision is preferred but this is varied, depending on the size and structure of the knee and the associated internal derangement. In this regard, Basset's⁶ book is instructive. I avoid curved or cross incisions and injury to the medial or lateral ligament and, if possible, the patella or patellar ligament. However, in elderly persons with marked osteo-arthritis the entire patella has been removed as advocated by Mader.⁷

All bleeding points are carefully clamped or coagulated by the suction tip with the high frequency electrocautery.³ The joint is thoroughly inspected. The anterior end of the meniscus is freed with the acusector, the suction tip being held near to remove smoke and clear the view. Any bleeding points are carefully coagulated as this proceeds. The cartilage is then cut along its base, the vascular area being avoided. At first an insulated curved acusector was used but was found to be unsatisfactory. More recently the knife designed by Lowe and Breck⁸ has greatly facilitated this procedure. I have had no experience with the

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7. Mader, V. O.: A New Approach to the Knee Joint, *Canad. M. A. J.* 42:17 (Jan.) 1940.

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Mercer⁹ knife or with the use of the Leggiadro¹⁰ knife. The entire posterior portion is removed as advised by many authors, if necessary, through posterior incision. Damage to articular surfaces is carefully avoided, as is excessive manipulation of the joint. All enlarged or disturbed portions of the subpatellar fat pad are removed. The joint is thoroughly inspected for loose bodies, synovial villi, adhesions or other pathologic disturbances as suggested by MacAusland.¹¹ It is then thoroughly lavaged with the procaine solution, minus epinephrine, or physiologic solution of sodium chloride, the suction being used to prevent wetting of dressings. This is a simple apparatus, 9 inches long, made of number 30 stainless steel tubing, carrying a hose connection threaded on the proximal end, with a 4½ inch insulated handle. The distal end is slightly curved over the outer 2 inches, the tip being rounded, carrying a pin-sized central opening with four similar sized openings about the circumference of the tip. A small stilet of stainless steel wire, which can be passed through the central opening, is kept at hand to clean the small holes. There is a grooved metal collar at the upper end of the insulated handle which permits contact of the electrocautery point by the assistant. This simple instrument, properly handled, greatly reduces the operative time and loss of blood, keeping the field clear. Ordinary bleeding points touched with it are momentarily dried and the current coagulates them without charring; this reduces the amount of foreign material in the wound, promotes healing and greatly reduces the possibility of infection. In the deeper regions it is most convenient; quickly applied to bleeding points, it produces hemostasis with little trouble.

A blended spark gap and tube current is preferred.³ A good head lamp greatly facilitates the whole procedure.

Lavage with physiologic solution of sodium chloride washes up any loose bits of tissue, indicates any bleeding points, clears the wound of air-borne bacteria and prevents drying of the raw tissue surfaces.

Fingers are kept out of the wound as much as possible but, if necessary, exploration is carried out with a finger after washing the gloved hands with mercury bichloride solution. The joint is immediately afterward lavaged with physiologic solution of sodium chloride. Sponges are kept out of the wound. They are apt to leave lint within the joint, which forms minute foreign bodies. MacAusland¹¹ cautions against sponges.

The joint is then filled with physiologic solution of sodium chloride, which may be diluted with procaine hydrochloride; the synovium is carefully matted with fine black silk sutures, as are the remaining layers of tissue. The skin is closed with lock stitches of the same material. Alcohol soaked gauze is placed over the wound and covered by wrappings of sterile glazed cotton. The entire leg and posterior portion of the foot are encased in a light plaster splint or crinoline and strips of basswood, with this dressing moderately snug about the knee. Some of the joints have been closed and air injected before the dressings were applied; this or the fluid, with moderate pressure of the outer dressings, reduces the possibility of chance hemorrhage from any of the coagulated points.

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CONVALESCENCE

When local anesthesia is used, sweating, shock and loss of fluid associated with general anesthesia is avoided, likewise the break in food intake, all of which shortens convalescence and greatly reduces postoperative complications. The patient is permitted to sit up in bed the same day and is allowed up in a wheel chair on the third day with the affected leg horizontal. Many patients are permitted crutches on the fifth day. The splint is removed on the sixth or seventh day; also the stitches. The joint is then aspirated of any fluid and its character noted. From 20 to 40 cc., or a sufficient amount, of air is then injected to produce moderate pressure. Both passive and active motions are started. Increments of activity with regard to amplitude of motion and weight bearing are gradually and steadily increased. Patients who do not have complications bear almost their full weight on the twelfth day and use a cane on the fifteenth day. Many have been returned to full activity with no disability three weeks from the day of operation, with no synovial thickening or disturbance other than slight tenderness about the operative scar.

Injection of air is of great help in convalescence. If hemorrhage has occurred, a sufficiently large bore needle to remove it is employed. The joint may be lavaged with physiologic solution of sodium chloride through this needle until the fluid returns quite clear, when air is injected to act as a cushion. Fluid is not compressible while the air cushion prevents adhesions, adds to comfort¹ and permits greater and earlier mobility. Occasionally it is necessary to aspirate and inject a second time. MacAusland¹¹ nine years ago remarked on the stiffness of a joint resulting from hemorrhage. A number of patients treated in the manner described on postoperative aspirations have shown no abnormal amount or character of synovial fluid and invariably progressed to an early and complete recovery with no disability. Some of them have been carpenters, one of whom returned to full occupation on the eighteenth day after operation. Patients who do not have complications receive no physical therapy.

COMMENT

In this group of fifty cases no infection of a joint occurred. Two elderly women developed superficial stitch abscesses in the subcutaneous fatty tissues; since then stay sutures of silkworm gut have been employed instead. Twenty-six were uncomplicated cases with a hospital stay ranging from a minimum of three days to a maximum of seven. Total disability of eighteen days in one case ranged to three or four weeks; in others, up to a maximum of six weeks, females invariably progressing more slowly than males. Five females did not have complications. The maximum postoperative temperature in this group was 100.8 F. and was of short duration.

Three of the fifty cases were misdiagnosed and at operation found to be simple osteochondritis dissecans, one chondromalacia patellae and one a congenital malformation with a band of tissue snapping across the upper portion of the external condyle. One proved to be multiple chondromas, another osteochondromas with alcaptonuria. Still another was complicated by a cyst of the external cartilage and five with osteoarthritis; one by a loose body. There were five cases associated with fracture of the head of the tibia or of the condyles. Ages ranged from 8 to 61 years. Those

cases complicated by fracture or arthritis were much slower to recover and required physical therapy.

Three were complicated by hemorrhages due to blood dyscrasias, one of which responded immediately to vitamin K therapy. One peculiar case with a history of purpura and previous hemarthroses, with a very peculiar blood picture, did not respond to the administration of vitamin K, food changes or other vitamin therapy, except that the general appearance improved. The first case in which there was extensive postoperative hemorrhage occurred early in the series; there was profuse bleeding at operation and the knee joint filled with blood after operation and on aspiration a week later again refilled. Convalescence was slow, requiring three or four months, but the patient eventually obtained a knee with normal range of fairly smooth motion. In one case acute appendicitis developed the second day after operation and one was complicated by carcinoma of the uterus. One knee was opened following a second injury which damaged the external meniscus a year after removal of the internal meniscus. This joint was found to be free of adhesions and normal in every respect; there had been some regeneration of fibrous tissue along the base of the internal semilunar cartilage.

Three of the uncomplicated cases were investigated by arthroscopy a year or more following operation and the joints were found to be quite normal. This is in sharp contrast to six knees which have been investigated by exploratory arthrotomy a year or more following operation under tourniquet when the joints were known to have contained a fair amount of blood following operation. Synovial surfaces were found with many adhesions, with diminution of the joint space. Two were found to have tags or apron-like hypertrophied areas of synovial membrane associated with adhesions. These joints all presented varying amounts of limited motion before the second operation, and convalescence following it was prolonged and varying grades of joint disturbance persisted.

Boppe¹² reviewed the procedure of some twenty-one surgeons over the world eight years ago. At that time Porter allowed weight bearing in three days, others in seven, eight and nine, while most permitted weight bearing in from ten to fifteen days with full use by Henderson as early as seven days; but the majority of surgeons preferred about twenty days. A few cases respond well to early movement, weight bearing and activity. Age, weight, the general state of nutrition and the duration and extent of injury are all factors bearing on the rate of progress. Violent early motion may produce hemorrhage in the line of incision or within the joint, complicating recovery.

CONCLUSIONS

I believe that:

1. Local anesthesia is preferable to spinal or general anesthesia.
2. A thorough study of the patient should be carried out before operation.
3. A tourniquet should not be employed.
4. Complete hemostasis should be obtained.
5. Postoperative aspiration followed by injection of air greatly aids recovery.
6. Passive and active motion and function should be established early.

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¹² Boppe, Marcel, and others: The Operative Treatment of Fractured or Displaced Semilunar Cartilage, *J. Bone & Joint Surg.* 14: 229 (April) 1932.

ABSTRACT OF DISCUSSION

DR. ALAN DEFOREST SMITH, New York: Carefulness in preparing patients for operation and attention to details in the operation and postoperative care are to be commended. I have not found it necessary, however, to take many of the elaborate precautions which Dr. Bohlman uses, and I believe that they tend to make the treatment of this condition unnecessarily complicated. I have been hesitant about injecting air into knee joints as a routine procedure, because of the possibility of air emboli. Aspiration of the joint after operation in cases in which there is marked swelling, in order to remove the accumulated blood, is a useful procedure and should be practiced oftener. Hemorrhage after operation is nearly always due to incomplete hemostasis and not to a dyscrasia in the blood clotting mechanism. Operation in every case of internal derangement of the knee, no matter how strongly the symptoms and physical signs may point to a damaged meniscus, is to some degree an exploratory arthrotomy, because there are so many conditions which may complicate or simulate this lesion. I therefore feel that it is necessary to make a generous incision in order that the joint may be explored thoroughly. Dr. Bohlman agrees with the necessity for exploration but nevertheless prefers a short incision. It seems to me that exploration is facilitated by the use of a tourniquet, and I do not believe that this materially increases the likelihood of hemarthrosis after operation, if the tourniquet is removed before the incision is closed and if the bleeding points are ligated. The use of the coagulating current in accomplishing this is certainly helpful. Separate suture of the synovial membrane is in my opinion an important point in securing hemostasis. This has been mentioned by Dr. Bohlman. A number of authors support Dr. Bohlman in his contention that the entire cartilage should be removed. It has not been my practice to attempt removal of the posterior fourth or fifth of the meniscus, which ordinarily cannot be reached without a separate posterior incision, and I am quite certain that this small posterior tab has not resulted in any subsequent difficulty in these cases. Probably no harm is done by applying a splint for a period of a week after operation; I have preferred not to do this but to start motion the day after operation. In spite of what is said about the disadvantages of passive motion, I believe that if this is carried out carefully and gently for a few days until the patient can initiate active movements it helps greatly and practically always adds to his comfort as well as to the early mobility of his joint. I agree with Dr. Bohlman that early weight bearing is possible and desirable. The routine which I have outlined has been used in a large series of cases at the New York Orthopaedic Hospital, and in a follow-up study of 175 cases by Dr. Lantzounis no case of residual stiffness of a joint was found.

DR. PHILIP LEWIN, Chicago: Dr. Bohlman's recommendations were that: 1. Local anesthesia is preferable to spinal or general anesthesia. 2. A thorough study of the patient should be carried out before operation. 3. No tourniquet should be employed. 4. Complete hemostasis should be obtained. 5. Postoperative aspiration and injection of air greatly aids recovery. 6. Passive and active motion and function should be established early. I should like to ask Dr. Bohlman what an acusector is. I want to correct something he quoted from an earlier paper, that Porter was allowing weight bearing in three days. I can assure you that none of his patients were allowed to bear weight in three days. Regardless of whether Porter put in the questionnaire that he was letting them up in three days, or whether it was misquoted, the statement isn't true. I call your attention to a few random notes with regard to atrophy of the quadriceps muscle. There are two muscles in the body that atrophy when anything happens around them, whether disease occurs or especially if they are injured: one is the deltoid, the other the quadriceps extensor. They seem to begin quickly to atrophy. Let me call attention to a certain preoperative position for x-ray examination known as the Bécclère-Holmblad position. One usually says to the x-ray man "We want an A. P. and a lateral." I always insist on three if the patient can be put in the third position. The Bécclère-Holmblad position is one in which the patient kneels on a chair with the knee in a position of about 120 degrees of extension and the central ray is passed through

from behind. If you will do that in every case you won't miss any of these cases of osteochondritis dissecans that were mentioned in the author's paper. About preoperative exercises, I think it is important to tell the patient who is going to have an operation on his knee that he must practice using his quadriceps before the operation. There was a time when I used to give patients a typewritten slip saying "You must practice exercising your quadriceps before the operation because as soon as you wake up from the anesthesia (if it is a general anesthetic) I am going to insist that you raise your heel off the bed regardless of how much or how little pain it causes you." I tell them to tighten the knee, point the toes and raise the heel off the bed. They can do it with only one muscle and that is the quadriceps. If they are used to it before the operation and are thinking about it when going under the anesthetic, it is easy to get them to do it afterward. Postoperatively, they must elevate it whether they have a cast on or not, and if one has a compression cast on, they elevate that straight leg easier than if they have a pressure bandage on.

DR. HAROLD R. BOHLMAN, Baltimore: With regard to Dr. Smith's comment on air embolus, we feel pretty safe in this field. In none of these cases have we had embolism occur, even when we put in air immediately after operating, before we put on the dressings. The human body will tolerate a certain amount of intravenous air. Firor some years ago demonstrated that a dog could tolerate from 18 to 25 cc. of air in his venous system without great difficulty. I have had two cases of air embolism occur in gonorrheal arthritis joints, one of which I tried to distend when adhesions were present and another in which the joint space had been partially obliterated and I used too much tension. The immediate results were startling and very embarrassing to the patient and to the doctor as well, but neither resulted in a fatality. A number of these have been reported in the literature. I once suffered one bit of experience with air emboli in my veins while giving blood for a transfusion and somebody hooked up the vacuum pump in reverse. It was startling to feel the air gurgling up my brachial vessels; it raised my blood pressure and pulse rapidly but did no harm, although it gave me a bad start for a little while. With regard to Dr. Lewin's question on the acuator, that may not be a good term. I have forgotten who used it first, but I use it in association with a small knifelike instrument which has an insulated handle and is hooked up to a machine with a current of radio frequency characteristics. I refer to the Burdick machine, which I believe has a blended spark gap and tube current; for information on this, I refer you to Ward and Kelly's book on electrosurgery, which was published some eight years ago. Quadriceps atrophy I think depends a good deal on the duration of the disability before operation. In the oldest case in this series there were symptoms of twenty-five years' standing. The internal semilunar cartilage was badly chewed up and distributed about the joint, many pieces attached to the synovial membrane, as Timbrel Fisher notes loose bodies often do. This patient had a great deal of atrophy of the quadriceps muscle, but it came back surprisingly fast after a quarter of a century of disability of that knee. It was amazing to see how rapidly, without any particular help on our part, the quadriceps developed form and function.

Vitamin C.—Most animals do not get scurvy, however badly they are fed. They can make their own vitamin C, as the ascorbic factor is called. But monkeys and guinea pigs need it like men. And when Holst and Frölich produced scurvy in guinea pigs in Norway in 1907 it soon appeared that it was due to lack of a substance needed in small amounts; and the quantities in different foods could be roughly measured in doses needed to cure a guinea pig. I was in the next room when Szent-Györgyi, a Hungarian working at Cambridge, isolated vitamin C. He was not looking for it and did not know that his crystals were the vitamin. He had tracked down and purified a substance found in various plants and concerned in oxidations inside the cells of both plants and animals, where it plays a part somewhat like that of hemoglobin in the animal body as a whole.—Haldane, J. B. S.: *Science and Everyday Life*, New York, Macmillan Company, 1940.

COMPENSATORY ATROPHY OF THE ADRENALS

HANS SELYE, M.D.

MONTREAL, CANADA

It is well known that following partial removal of an endocrine gland the remaining parts of the organ tend to compensate for the loss by undergoing active hypertrophy and hyperplasia. This phenomenon has been referred to descriptively as compensatory hypertrophy. The isolation of purified hormone principles made it possible to study the effect of hormone overdosage on endocrine glands, and it soon became evident that in most cases excessive treatment with a certain glandular substance resulted in the eventual atrophy of the cells which normally have the task of producing this glandular product. It is not within the scope of this com-

TABLE 1.—*The Action of Desoxycorticosterone Acetate on Adrenal Weights in the Rat*

Material Injected	Number of Rats	Sex	Length of Treatment, Days	Body Weight, Gm.	Adrenal Weight, Mg.	Significance of Weight Change *
Oil.....	6	♂	10	152	39	Control
Desoxycorticosterone acetate.....	6	♂	10	152	20	P = <0.01
Cholesterol.....	6	♂	20	150	40	Control
Desoxycorticosterone acetate.....	6	♂	20	150	20	P = <0.01
Normal not injected....	6	♂	20	150	38	Control
Normal not injected....	6	♀	20	116	63	Control
Cholesterol.....	12	♂	20	157	39	P = 0.5
Cholesterol.....	12	♀	20	117	44	P = 0.1
Desoxycorticosterone.....	6	♂	20	150	19	P = <0.01
Desoxycorticosterone.....	6	♀	20	122	22	P = <0.01
Pregnanediol.....	5	♂	20	165	38	P = 0.8
Pregnanediol.....	5	♀	20	124	49	P = 0.3
Δ ⁴ -dehydro-iso-androstosterone.....	5	♂	20	163	36	P = 0.2
Δ ⁴ -dehydro-iso-androstosterone.....	5	♀	20	124	38	P = 0.01
Δ ⁴ -pregnenol-3-one-20....	5	♂	20	160	34	P = 0.4
Δ ⁴ -pregnenol-3-one-20....	5	♀	20	124	52	P = 0.1

* In all experiments reported in this paper, the significance of the apparent differences between the treated and control series was evaluated by "Student's" method for small samples (Fisher, R. A.: *Statistical Methods for Research Workers*, ed. 5, London, Oliver & Boyd, 1936, p. 128) and is expressed in terms of probability, estimated by graphic interpolation in Fisher's table of t. In accordance with the usual convention, differences between series cannot be accepted as significant when P is greater than 0.05. In each series the untreated animals or, in case all animals were injected, only the groups receiving oil or cholesterol were used as controls, since treatment with the latter substances proved ineffective in causing a change in the adrenal weight.

munication to review the extensive relevant literature. Suffice it to mention that the thyroid gland undergoes involution under the influence of an overdose of a thyroid preparation,¹ the pancreatic islets, especially the insulin producing beta cells, involute following treatment with insulin,² the ovaries after administration of estrogen³ or progesterone,⁴ the testis after androgen

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Owing to lack of space, this article has been abbreviated by omission of some of the illustrations. The complete article appears in the author's reprints.

Read before the Section on Pathology and Physiology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

The expenses of this work have been defrayed through a grant received from the Schering Corporation of Bloomfield, N. J. Drs. Gregory Stragell and E. Schwenk of this corporation supplied all the steroids used in this work except the pregnanediol, which was donated by Ayerst, McKenna and Harrison through the courtesy of Dr. Stanley Cook. The photomicrographs have been prepared by Mr. K. Nielsen and the microscopic slides by Mr. C. Rasmussen.

1. Loeb, Leo; Bassett, R. B., and Friedman, H.: *Proc. Soc. Exper. Biol. & Med.* **28**: 209 (Dec.) 1930.
2. Muggia, Aldo: *Arch. per le sc. med.* **50**: 185, 1927. Miyari, S.: *Mitt. d. med. Gesellsch. zu Tokyo*, 1928, vol. 42, No. 7.
3. del Castillo, E. B., and Calatroni, C. J.: *Rev. Soc. argent. de biol.* **6**: 108, 1930. d'Amour, F. E.: *J. Biol. Chem.* **92**: 1xxxv (June) 1931.
4. Selye, Hans; Browne, J. S. L., and Collip, J. B.: *Proc. Soc. Exper. Biol. & Med.* **34**: 472 (March) 1936.

therapy,⁵ the parathyroids after administration of solution of parathyroid⁶ and the adrenal cortex after administration of adrenal cortex extract⁷ or desoxycorticosterone.⁸ Even the pituitary shows degenerative changes in animals chronically treated with hypophysial extracts.⁹ It appears logical to refer to this atrophy as "compensatory atrophy," since it is the exact antithesis of compensatory hypertrophy and appears to be the result of a readjustment of endogenous hormone production in an organism which is flooded with an exogenously introduced glandular preparation. In the case of the endocrine glands which stand under the regulating influence of the pituitary, it is most probable that compensatory atrophy is due to a decrease in the elaboration of the corresponding tropic hormone. This is shown by the fact that estrogens cause no atrophy in hypophysectomized animals whose ovaries are maintained by daily injections of gonadotropic substance,¹⁰ and cortical preparations fail to cause cortical atrophy in intact rats receiving adrenotropic substance by injection.¹¹

If the phenomenon of compensatory atrophy, as defined, is considered from the point of view of its clinical significance, it is evident that it could never serve to inhibit an excess production of hormone by an endocrine organ since, in order to produce atrophy of an overfunctional gland, one would have to administer a further excess of the same endocrine substance which is already present in unusually large amounts in the circulation of the patient. In such cases the possible benefit which could be derived from the inhibitory action exerted by the hormone on the overactive gland is outweighed by the damage which would be produced by aggravating the existing endocrine overdosage. Yet the endocrine treatment of diseases of hormone oversecretion would appear to be of the greatest clinical significance, since, in spite of all the progress made in the substitution therapy for hormone deficiencies, elimination of the hyperactive gland by surgical means or roentgen therapy are still the only reliable methods of coping with diseases of excess production of hormone.

In view of these considerations, an effort was made to determine whether treatment with glandular substances chemically similar to but physiologically different from those produced by a gland of internal secretion could also result in its compensatory atrophy. It was felt that if this should be the case it might open new methods of therapy, because the direct peripheral effects of the introduced substance would be different from those of the hormone elaborated by the hyperactive gland and would not necessarily aggravate the existing condition of overproduction of hormone.

The discovery that either estrogenic or androgenic substances may cause gonadal atrophy in both sexes,¹² which fact was confirmed with crystalline synthetic androgens and estrogens,⁸ was an encouraging indication that at least in certain cases such a "transferred compensatory atrophy" is possible. However, in this instance the resulting atrophy is most probably due to the inhibition of gonadotropic hormone production, and since the latter is responsible for the maintenance of both ovary and testis it appeared possible that we are dealing with a rather unique example. Yet in cases of excessive estrogen production (e. g. women in the menopause), inhibition of ovarian function by androgens or progesterone (which, as was said, also causes ovarian atrophy) may prove of therapeutic significance. Another observation that may perhaps be interpreted as an example of transferred compensatory atrophy is the observation of de Fremery,¹³ who found that diiodotyrosine causes the normally active thyroid glands of immature rats to assume the resting type. The fact that this inhibition is not due to a direct action on the thyroid is well shown by the fact that the "resting" thyroids of rats treated with diiodotyrosine remain so sensitive to exogenously introduced thyrotropic preparations that the author recommended animals so treated

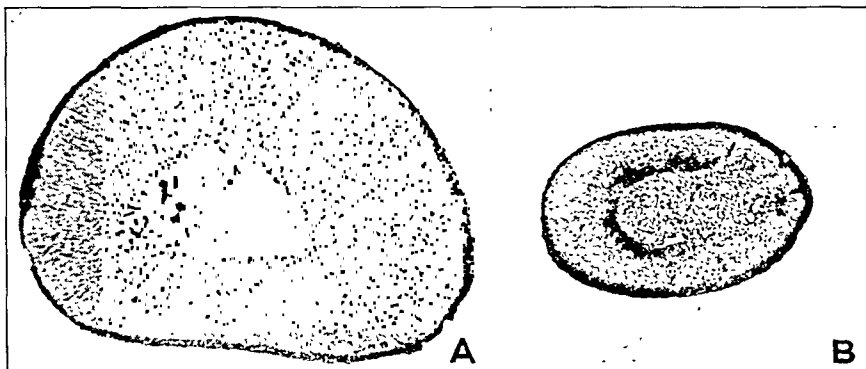


Fig. 1.—A, low magnification of cross section through adrenal of normal control female rat. B, low magnification of cross section through adrenal of female rat treated with desoxycorticosterone acetate. Note marked involution of the cortex while the medulla is but slightly subnormal in size.

to be used for the bio-assay of thyrotropic extracts. It appears quite possible that the diiodotyrosine molecule, which differs but slightly from that of thyroxine, retains the latter's ability to cause compensatory thyroid atrophy though it loses its other physiologic actions.

In the present communication I report a series of experiments in which the compensatory atrophy of the adrenals was submitted to a systematic study. This appeared especially interesting since the adrenal produces a large number of hormone principles, many of which are available in pure crystalline form. It was thought, therefore, that this gland would furnish an excellent test object on which to study the question of whether overdosage with one hormone principle made by a certain cell could inactivate this cell sufficiently to prevent it from producing not only this but also the other hormones which it usually elaborates.

THE ACTION OF DESOXYCORTICOSTERONE

Among the investigators who studied the action of life-preserving adrenal cortex extracts on the adrenals, some claimed that these produce no significant change¹⁴

5. Korenchevsky, V.; Dennison, M., and Kohn-Speyer, A.: *Biochem. J.* **27**: 557, 1933. Schoeller, W., and Gehrke, M.: *Biochem. Ztschr.* **264**: 352, 1933.

6. McLunkin, F. A.; Tweedy, W. R., and Breuhau, H. C.: Parathyroid Hormone: Its Regulatory Action on Parathyroid Glands and Toxic Effect on Tissues of Rat, *Arch. Path.* **14**: 649 (Nov.) 1932.

7. Ingle, D. J., and Kendall, E. C.: *Science* **86**: 245 (Sept. 10) 1937.

8. Selye, Hans: *Canad. M. A. J.* **42**: 113 (Feb.) 1940.

9. Collip, J. B.; Selye, Hans, and Thomson, D. L.: *Proc. Soc. Exper. Biol. & Med.* **31**: 682 (March) 1934.

10. Selye, Hans, and Collip, J. B.: *Endocrinology* **20**: 667 (Sept.) 1936.

11. Ingle, D. J.; Higgins, G. M., and Kendall, E. C.: *Anat. Rec.* **71**: 363 (July 25) 1938. Ingle and Kendall.⁷

12. Moore, C. R., and Price, Dorothy: *Am. J. Anat.* **50**: 13 (March) 1932.

13. de Fremery, P.: *Acta brev. Neerland.* **5**: 35, 1935.

14. Lippross, O.: *Endokrinologie* **18**: 18, 1936. King, J. L.: *Proc. Soc. Exper. Biol. & Med.* **35**: 619 (Jan.) 1937.

plete disappearance of the X zone (figs. 6 and 7A). It appears therefore that this compound, which is not a testis hormone, is capable of causing involution of the presumably androgenic zone. If it should prove correct that the X zone is functionally different from the remaining cortex and is the source of adrenal androgens, one would have to consider this change to be

TABLE 2.—*The Action of Desoxycorticosterone Acetate on Adrenal Weights in Mice*

Material Injected	Number of Mice	Sex	Body Weight, Gm.	Adrenal Weight, Mg.	Significance of Adrenal Weight Change *
Not injected.....	6	♂	24	3.5	—
Not injected.....	6	Castrate ♂	20	3.7	P = 0.6
Cholesterol.....	6	Castrate ♂	21	3.2	P = 0.5
Desoxycorticosterone acetate	6	Castrate ♂	21	2.7	P = 0.04
Not injected.....	6	♀	22	4.8	—
Not injected.....	6	Spayed ♀	21	4.7	P = 0.7
Cholesterol.....	6	Spayed ♀	23	4.4	P = 0.3
Desoxycorticosterone acetate	6	Spayed ♀	21	2.6	P = 0.03

* The significance of the apparent differences has been calculated, the noninjected castrates being used as controls for the treated castrates and the noninjected intact animals as controls for the noninjected castrates.

another example of "transferred compensatory atrophy." In any case the microscopic appearance of the cortical cells was such in all zones of the organ that it seems very probable that their ability to produce hormones other than desoxycorticosterone was likewise impaired, the atrophy appearing to be "transferred" even in this respect.

THE ACTION OF PROGESTERONE

Using relatively small doses (2 mg. a day) of progesterone, I⁸ obtained only slight adrenal atrophy in female rats and none in males. Clausen²⁵ was unable to produce a statistically significant decrease in the adrenal weights in this species, but this might have been due to the fact that he used relatively small doses. In the mouse, Starkey²⁶ asserted, without having experimental evidence to support his assertion, that progesterone might cause involution of the X zone. This has been contradicted by Martin,²⁷ Tolenaar²⁸ and Howard,²² who stated that progesterone in daily doses up to 5 mg. causes no change in the X zone of the adrenal in immature mice. Hence it was concluded that this hormone cannot be made responsible for the physiologic involution of this zone during gestation.

In view of the fact that the experiments mentioned in the previous section showed definitely that desoxycorticosterone causes marked adrenal atrophy, it appeared of special interest to establish whether progesterone, which differs from the latter only in the absence of one -OH group on C atom 21, would have the same effect. For this purpose 12 female albino rats weighing on the average 107 Gm. were divided into two groups of 6. The first group received only 0.4 cc. of peanut oil subcutaneously daily; the second group was injected with 10 mg. of progesterone in the same amount of oil. After twenty days of treatment, all animals were killed. The average adrenal weight in the control group was 40 mg. at this time, while in the progesterone-treated group it was only 29 mg. This decrease is obviously statistically significant since $P = < 0.01$. Another experiment of this type was performed on 12 castrate male albino rats weighing 175 Gm. on the

average. Here again 10 mg. of progesterone was administered daily in 0.4 cc. of peanut oil to one group while the other group was treated merely with peanut oil. The average adrenal weight was 40 mg. in the controls and 36 mg. in the progesterone-treated group. However, this decrease was not statistically significant since $P = 0.3$. The reason progesterone failed to cause more significant atrophy in this group is probably that these animals were much heavier than those of the previous group and yet received the same dose of the substance. Several other experiments in which we studied the action of progesterone confirmed these observations, as they showed that this compound causes some decrease in adrenal weight but is much less potent in this respect than desoxycorticosterone.

In 6 gonadectomized female albino mice having an average body weight of 21 Gm., daily administration of 3 mg. of progesterone caused a decrease in the average adrenal weight from 4.7 to 3.8 mg. ($P = 0.05$), while in 6 males of the same size the average adrenal weight of the noninjected castrates (3.7 mg.) was approximately the same as that of the progesterone-treated animals (3.9 mg.). These results confirm the view expressed in our previously quoted paper, namely that the female organism is more sensitive to this action of progesterone than the male. At the same time a comparison of the atrophy produced in these groups with the decrease in adrenal weight caused by treatment with desoxycorticosterone acetate under exactly identical conditions (see the previous section of this communication) shows beyond doubt that the slight change in the molecular structure of desoxycorticosterone which results in its transformation into progesterone greatly reduces its ability to cause adrenal atrophy.

Microscopic studies of the adrenals of progesterone-treated rats showed lesions which were essentially similar to those elicited by desoxycorticosterone but were much less pronounced. In the gonadectomized

TABLE 3.—*Inhibition by Various Steroid Compounds of the Adrenal Hypertrophy Caused by Estradiol*

Material Injected	Number of Rats	Sex	Adrenal Weight, Mg.	Significance of Adrenal Weight Change *
Not injected.....	6	♂	35	Control
Estradiol.....	6	♂	48	P = < 0.01
Estradiol and progesterone.....	6	♂	39	P = 0.03
Estradiol and testosterone.....	6	♂	41	P = < 0.01
Estradiol and desoxycorticosterone acetate.....	6	♂	39	P = 0.02
Not injected.....	6	♀	42	Control
Estradiol.....	6	♀	48	P = 0.1
Estradiol and progesterone.....	6	♀	47	P = 0.1
Estradiol and testosterone.....	6	♀	43	P = 0.5
sterone acetate.....	6	♀	46	P = 0.7

* The statistical significance of the apparent change in adrenal weight is expressed in comparison with the noninjected normals in the case of the animals treated with estradiol alone. In all other cases the result of combined treatment with two compounds is compared with that of mere estradiol administration.

mouse, the most conspicuous result of progesterone therapy was the disappearance of the X zone in both sexes (fig. 7B).

THE ACTION OF ANDROGENS

While most investigators agree that the X zone of the mouse adrenal disappears under the influence of androgens,²⁹ no significant change in the weight or histologic structure of the adrenal has been observed

25. Clausen, H. J.: Read before the meeting of the American Association of Anatomists, Louisville, Ky., March 20-22, 1940.

26. Starkey, W.: Univ. Pittsburgh Bull., October 1937, vol. 34.

27. Martin, S. J.: Proc. Soc. Exper. Biol. & Med. 28: 41, 1930.

28. Tolenaar, J.: Acta brev. neerl. 9: 54, 1939.

29. Poll, Heinrich: Deutsche med. Wchnschr. 59: 567 (April 14) 1933; Anat. Anz. 77: 113, 1933. Martin.²⁷ Howard.²²

in lizards,³⁰ guinea pigs³¹ and dogs.³² Vidgoff and Vehrs³³ stated that in the rat the so-called inhibitory hormone of the testis, which causes involution of the male sex organs, leads to hypertrophy of the adrenal cortex. However, I³⁴ demonstrated that all nonspecific agents which cause gonadal atrophy also produce enlargement of the adrenal cortex, and therefore it appears very probable that the relatively crude testis extracts employed by Vidgoff and Vehrs owe both their adrenal enlarging and sex organ inhibiting actions to their toxicity. Crystalline testosterone causes definite adrenal atrophy in immature females³⁵ and a less pronounced decrease in adrenal weight in adult females,³⁶ but no such decrease could be obtained in adult males.⁸ It is of interest that in the case of early postnatal treatment with testosterone propionate the cortical atrophy is particularly marked in the rat but is due mainly to involution of the glomerulosa.³⁷ In this respect the atrophy differs qualitatively from that produced by hypophysectomy, which, as I mentioned before, is characterized by a predominant reticularis atrophy.

Since the adrenals are smaller in males than in females, the fact that a definite decrease in adrenal weight was obtained only by androgens in female rats might be regarded as an indication that this change is due merely to a "masculinization" of the female. In order to test this possibility my associates and I performed an experiment in a group of 12 newborn albino male rats, 6 of which received 1 mg. of testosterone daily during twenty-four days, beginning on the day of birth. The dose was then raised to 3 mg. daily, the animals being killed on the thirtieth day of treatment. The remaining 6 rats received the same dose of cholesterol during this period and served as controls. The experiment was performed on such immature animals because previous observations taught us that it is easier to inhibit the development of the adrenal than to cause atrophy of a fully developed gland. The average adrenal weight in the controls was 24 mg. as compared with 12 mg. in the testosterone-treated group. The decrease was obviously statistically significant, since even the largest adrenal in the testosterone group was considerably smaller than the smallest of the control glands ($P < 0.01$). This experiment indicates perhaps that one is dealing not merely with a "masculinization" but with true compensatory atrophy, although it is not impossible that the gonads of such

immature males produce so little—if any—androgen that the treatment may be regarded as "masculinization" of a neutral type.

Experiments on 6 castrate male and 6 spayed female 1 month old albino mice with an average body weight of 22 Gm. showed that daily administration of 3 mg. of testosterone during a period of twenty days caused no change in the average adrenal weight of the males (3.7 mg.), but in the females the average weight of the organ decreased from 4.7 to 3.8 mg. ($P = 0.06$). Microscopic examination showed that irrespective of the adrenal weight the X zone disappeared under the influence of the androgen in both sexes (fig. 8).

These results indicate that androgens have a definite effect on the adrenal cortex, a conclusion which receives further support through the observations recorded in table 1, that dehydro-*iso*-androsterone is also active in decreasing the adrenal weight of the female rat.

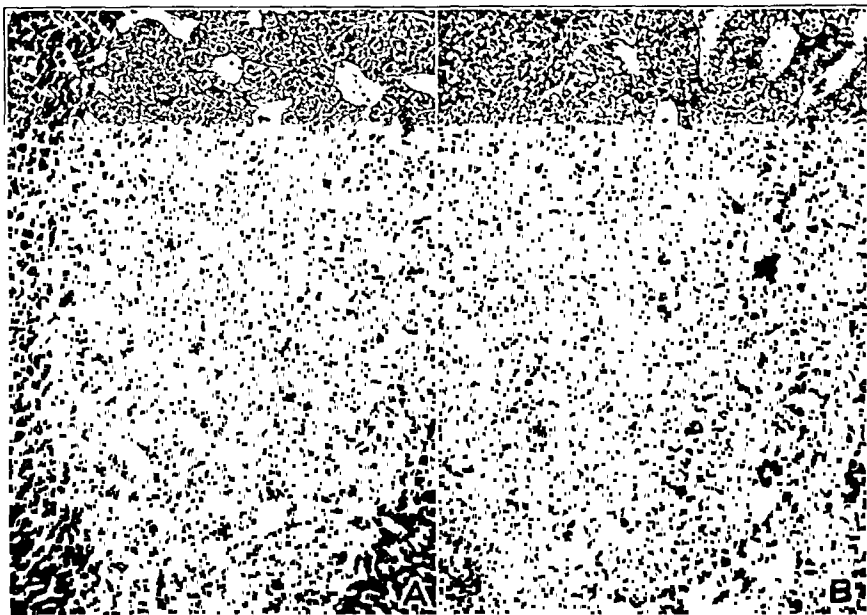


Fig. 5.—A, high magnification of medulla of normal control male rat. B, adrenal medulla of male rat treated with desoxycorticosterone acetate at same magnification as in A. Note marked vacuolization and involution of medullary cells.

PREVENTION OF VARIOUS TYPES OF HYPERTROPHY OF ADRENAL CORTEX BY MEANS OF STEROID HORMONES

Although early investigators who used impure preparations of estrogens obtained contradictory results,³⁸ Selye, Collip and Thomson³⁹ showed that crystalline estrone causes marked hypertrophy of the adrenal cortex in the rat, a fact which has since been confirmed for numerous other estrogens. It appeared of interest to establish whether this hypertrophy may be prevented by other steroid hormones. For this purpose a series of experiments was performed on albino rats. The average weight of the males was 154 Gm. and that of the females 109 Gm. All experimental animals were treated with daily doses of 300 micrograms of alpha-estradiol while the other steroid hormones were administered in daily doses of 2 mg. The daily dose of each of these com-

30. Forbes, T. R.: Read before the meeting of the American Association of Anatomists, Louisville, Ky., March 20-22, 1940.

31. Bottomley, A. C., and Folley, S. J.: *J. Physiol.* **94**: 26 (Oct. 14) 1938.

32. Nosaka, J.: *Folia endocrinol japon.* **12**: 26, 1936.

33. Vidgoff, Ben, and Vehrs, Herman: *Endocrinology* **26**: 656 (April) 1940.

34. Selye, Hans: *Endocrinology* **25**: 615 (Oct.) 1939.

35. McEuen, C. S.; Selye, Hans, and Collip, J. B.: *Proc. Soc. Exper. Biol. & Med.* **36**: 213 (March), 390 (April) 1937.

36. Korenchevsky, V.; Dennison, M., and Hall, K.: *Biochem. J.* **31**: 780 (May) 1937. Wolfe, J. M., and Hamilton, J. B.: *Endocrinology* **25**: 572 (Oct.) 1939. Mazer, Milton, and Mazer, Charles, *ibid.* **24**: 175 (Feb.) 1939. Selye, *ibid.*

37. Selye, Hans: *Anat. Rec.* **76**: 145 (Feb. 24) 1940.

38. Watrin, J.: *Compt. rend. Soc. de biol.* **92**: 1451, 1925. Montpelier, J., and Chiappini, L., *ibid.* **104**: 375, 1930. Shumacker, H. B., Jr., and Lamont, Austin: *Proc. Soc. Exper. Biol. & Med.* **32**: 1568 (June) 1935.

39. Selye, Hans; Collip, J. B., and Thomson, D. L.: *Proc. Soc. Exper. Biol. & Med.* **32**: 1377 (May) 1935.

pounds was injected subcutaneously in 0.1 cc. of peanut oil during a period of twenty days. The results of the experiments are summarized in table 3. The table indicates clearly that progesterone, testosterone and desoxycorticosterone are all capable of inhibiting the estradiol hypertrophy of the adrenal in males in which estradiol induced a significant cortical enlargement. In the females, the adrenals of which are larger than those of the males under normal conditions, the 300 microgram dose of estradiol used in these experiments led to no statistically significant adrenal weight increase and consequently the other steroids could not show a significant inhibition.

The fact that the adrenal enlargement normally produced by muscular exercise may be prevented by cortex extracts has been demonstrated by Ingle.²⁴ My associates and I⁴⁰ found that desoxycorticosterone, testosterone and progesterone may also prevent the adrenal enlargement caused by various other damaging agents such as injections of formaldehyde and surgical shock. Since during the alarm reaction elicited by such stimuli as muscular exercise, trauma or toxic doses of drugs the pituitary responds with an increase in adrenotropic hormone production¹⁰ and the aforementioned steroids inhibit the elaboration of the adrenotropic principle by the pituitary, it is concluded that the inhibition of adrenal enlargement under these conditions is probably mediated by the hypophysis.

SUMMARY AND CONCLUSIONS

Experimental evidence indicates that both in the mouse and in the rat desoxycorticosterone acetate causes marked involution of the adrenal cortex. Histologically the atrophy of the cortical cells is very pronounced in all three zones, yet unlike the atrophy caused by hypophysectomy it is not particularly severe in the zona reticularis. Although it appears quite probable that the action of this cortical steroid is due to its ability to inhibit production of adrenotropic hormone, this observation is not easily reconcilable with such an interpretation. The cells of the adrenal medulla become vacuolized and show signs of degeneration in rats treated with desoxycorticosterone acetate.

In the gonadectomized male or female mouse the characteristic X zone of the cortex disappears under the influence of desoxycorticosterone acetate. Changes in the medulla are not readily detectable in this species.

Progesterone given in large doses also causes involution of the adrenal cortex in the rat and to a lesser degree in the mouse. This effect is evident only in females, and even in these much higher doses have to be administered to obtain an atrophy comparable to that caused by desoxycorticosterone acetate. The X zone of the mouse adrenal disappears in gonadectomized males or females treated with progesterone.

Androgens such as testosterone or Δ^5 -dehydro-isoandrosterone are also capable of causing involution of the adrenal cortex, again much more readily in females than in males. The disappearance of the X zone, which is obtained by androgens in gonadectomized mice, is not always accompanied by a measurable decrease in adrenal weight.

Estradiol causes much more pronounced hypertrophy of the adrenal cortex in male than in female rats. This effect is inhibited by the simultaneous administration of desoxycorticosterone acetate, progesterone or testosterone.

The atrophy of an endocrine gland caused by the administration of an excess of the hormone or hormones which it produces is regarded as the exact antithesis of the compensatory hypertrophy elicited by the hormone deficiency occasioned by partial extirpation of such a gland. For this mechanism of readjustment the term "compensatory atrophy" is suggested. It is essentially the same mechanism which in human pathology is responsible for instance for atrophy of the adrenal cortex if a tumor develops in the cortex of the contralateral adrenal gland. Experimental work shows that such compensatory hypertrophy may in some instances be produced by substances other than the main product of secretion of a certain endocrine gland. Thus atrophy of the testis has been elicited with estrogens or progesterone, atrophy of the adrenal cortex with androgens or progesterone, involution of the adrenal medulla with desoxycorticosterone acetate and the like. In these cases, one is dealing with a "transferred" compensatory atrophy. This phenomenon promises to be of clinical importance, since it may afford a means by which to decrease the activity of overfunctioning endocrine glands without having to administer additional amounts of a substance which is already produced in excess. Thus, for instance, the use of desoxycorticosterone acetate (a substance which is practically devoid of androgenic activity) in cases of adrenogenital syndrome in which there is an excess production of androgen in the adrenal may prove useful in inhibiting the faulty endocrine secretion of the cortex.

ABSTRACT OF DISCUSSION

DR. J. P. SIMONDS, Chicago: Some years ago Dr. O. E. Hepler, working in our department on fat tolerance in experimental hyperthyroidism, demonstrated both anatomic and physiologic evidence of compensatory atrophy. After dogs had been fed large doses of desiccated thyroid for several weeks the thyroid gland became so small that it was often difficult to find it. When such feeding was stopped, the cholesterol of the blood rose within two weeks to the high levels characteristic of myxedema and other forms of hypothyroidism. I should like to ask Dr. Selye if he has made any observations on the permanence of this compensatory atrophy.

DR. MILTON STEINBERG, Chicago: I would mention in connection with this paper that in all probability the results were mediated through the anterior pituitary; that the results were not directly through flooding the system with the hormone but through suppressing the pituitary. I think that this work should be checked by examining the anterior pituitary microscopically and should also be checked in animals with the anterior pituitary removed; I doubt whether the effect would be present in that case.

DR. HANS SELYE, Montreal, Canada: With regard to the permanence of the lesions, I experimented only with testosterone and found that its actions are still detectable months after injections were discontinued. However, I don't believe the change would be permanent in the true sense of the word and I suppose that after a still longer period recovery would ensue. With regard to the statement that the adrenal atrophy induced by steroid hormones is indirect and mediated by the pituitary, I should like to state that this is quite in accordance with my own opinion; in fact, I have experimental evidence to prove this point. It was shown that if a hypophysectomized rat receives sufficiently large doses of adrenotropic hormone to maintain the adrenal in a normal condition, none of the steroids mentioned are able to cause cortical atrophy. This, I feel, shows distinctly that the steroids act mainly, if not entirely, by depressing the adrenotropic hormone secretion of the hypophysis. The only observation which would seem to plead against this interpretation is that the microscopic appearance of the cortex following atrophy induced by testosterone or desoxycorticosterone differs from that seen in hypophysectomized rats, a fact illustrated by the lantern slides.

40. Selye, Hans; Dosne, Christiane; Bassett, L., and Whittaker, J.: *Canad. M. A. J.* 43:1 (July) 1940. Selye.⁸

MULTIPLE BENIGN CYSTIC
EPITHELIOMA

REPORT OF TEN CASES IN ONE FAMILY

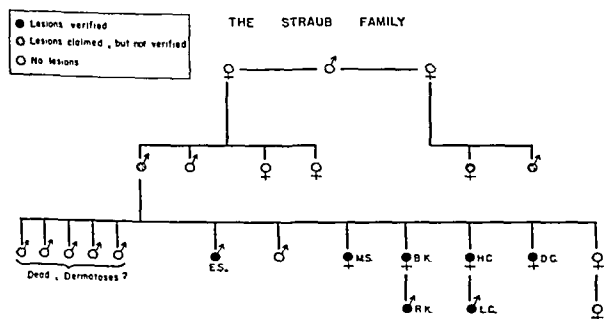
H. J. GOLDMAN, M.D.
ST. LOUIS

By this time the familial occurrence of multiple benign cystic epithelioma is a matter of general knowledge. As to the literature, the papers by Summerill and Hutton, by Sutton, by Beck, by Savatard and by Ricker and Schwalb supply sufficient details on the subject. A full bibliography appears in the articles by Summerill and Hutton and by Beck. The most extreme example was that of Sutton, who reported seventy-four cases in three generations. Of these, only one case was verified by biopsy; five were diagnosed by direct clinical examination and the remainder on hearsay. My own experience was made the more valuable because in seven of the ten cases a biopsy was secured—not only one specimen, but in one case three specimens and in three others two specimens. In short, twelve lesions taken from seven patients were studied. Thus it was possible to study, from one patient, a lesion from the angle of the nose, the forehead and the bridge of the nose and from another one from the lip and the scalp. This supplied an opportunity for comparison of lesions in one and the same patient as they occurred in different locations and to determine whether the processes were uniform in all the lesions.

It was a further stroke of good fortune that the family under study was a prolific one, numbering no fewer than sixteen members in the three generations affected by lesions. Moreover, the grandfather in the case had two wives, thus affording an opportunity to refer the hereditary factor to him and establish its transmission through two separate lines.

TRANSMISSION

The incidence of the condition in this family was 60 per cent. Whereas at first it was transmitted from the male to females, on subsequent occasions it was passed through the female. That is, there was not any consistent sex factor in the transmission of the disease.



MULTIPLE BENIGN CYSTIC EPITHELIOMA

Fig. 1.—The family tree.

The ratio of males to females was 5 to 5. Most strikingly, of seven brothers and sisters in the third generation whom I was able to study, five were affected.

Read before the Section on Dermatology and Syphilology at the Ninety-first Annual Session of the American Medical Association, New York, June 14, 1940.

From the Laboratory of Dermatological Research, University of Pennsylvania School of Medicine and the Graduate Hospital of the University of Pennsylvania.

HISTORY OF CASES

Mary S., aged 30, had distribution of the lesions as illustrated in figure 2. In addition there was a solitary lesion on the left shoulder. The disease began at the time of puberty. This case has been reported in full by Weidman and Besancon.¹ The lesion from in front of the ear exhibited the microscopic appearance of tricho-epithelioma, whereas the one from the shoulder exhibited syringo-adenoma.

Elmer S. (brother of Mary S.), aged 34, has had the disease twenty-five years. The distribution is indicated in figure 3.

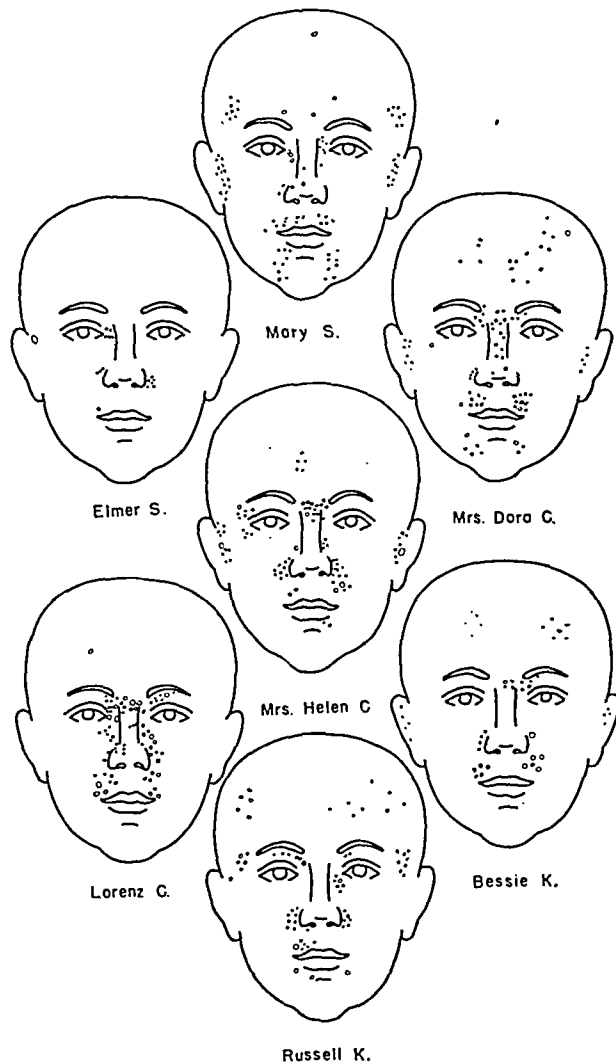


Fig. 2.—Distribution of lesions in the seven cases. Mary S. had a solitary syringo-adenoma on the left shoulder in addition. Note the large lesion on the scalp of Russell K.; there were also lesions back of the ear.

A lesion from in front of the ear exhibited the microscopic appearance of tricho-epithelioma. There were numerous large keratinous nests. The same order of process was exhibited in a lesion from the angle of the nose. Incidentally, the cells in the first lesion contained much fine granular pigment.

Mrs. Dora C., aged 32, the married sister of Mary S. and Elmer S., had onset of the condition at puberty. Three specimens of lesions were secured. In those from the angle and the bridge of the nose the picture was identical, featuring numerous keratinous nests (probably dilated hair follicles). Foreign body granulomas were also present. In the third lesion, from the forehead, the picture was essentially that of a basal cell cancer, with one exception. Thus many of the

1. Weidman, F. D., and Besancon, J. H.: Histologic Differences in a "Syringoma" of the Face and Shoulder: Employment of Wax Reconstruction. Arch. Dermat. & Syph. 21: 279 (Feb.) 1930.

but this point cannot be stressed because the pigmentation did not occur consistently in the sections of my series.

In addition to the commonly postulated sites of predilection for lesions, the region in front of the ear should be noted.

4500 Olive Street.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: Beginning with the discovery of one of these patients, Dr. Goldman was led to a good deal of detective work, whereby he was able to follow down the rest of the family. As a result, a rather unusual experience was met; namely, no less than 12 specimens were secured for biopsy from no less than 7 different patients. To some extent, different histologic pictures were met, and yet all of them came from the same biologic strains; that is, brothers and sisters. It seemed reasonable, therefore, to assume that all of the pathologic processes were biologically similar and, as a matter of fact, clinically they were the same entities. They were not basal cell cancers; clinically they behaved like multiple benign cystic epithelioma. That gave an excellent opportunity for reconciling and comparing the biologic with the morphologic aspects. Too much dependence cannot be placed on the microscopic appearance in appraising the biologic phenomena in the situation, which at once brings up a most practical consideration. The conclusion is, as shown by the last photomicrograph in Dr. Goldman's presentation, that a lesion which microscopically appears to be basal cell cancer is not cancer at all—at least biologically. Let me illustrate this lesson by an example. Suppose one encounters a solitary lesion clinically in which most of the microscopic picture is that of basal cell cancer. What is one going to do to determine whether the prognosis is going to be that of basal cell cancer or that of multiple benign cystic epithelioma? This is the crux; namely, that search should be made for evidence of these keratinous nests. If they are large and conspicuous, there is no difficulty at all; the matter is settled. Such nests indicate a relationship with tricho-epithelioma and from that a benign prognosis. It may be that instead of the nests being large they will be small and may have to be searched for. It may be that one would have to examine sections from different levels of the same paraffin block and perhaps it would not be a bad policy in all of our cases of basal cell cancer to examine sections from several different levels of the block in order to determine whether any of these telltale collections of keratinous material are here or there. If one finds them, the prognosis is better. If they are not found and if reasonable care has been taken to secure an examination of different levels—that is, representative positions in the same lesion—then, and then only, can one assume that the diagnosis is basal cell cancer and that therefore the less favorable prognosis must be added.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I agree essentially with what Dr. Weidman has emphasized. A few years ago Dr. A. E. Ingels in a case report (*Epithelioma Adenoides Cysticum with Features of Syringoma*, *Arch. Dermat. & Syph.* 32:75 [July] 1935) demonstrated all types of transition between epithelioma adenoides cysticum, tricho-epithelioma and syringoma. I have seen other cases in which there were similar transitions to cylindroma. Nomland reported a case that clinically resembled multiple benign pigmented nevi but histologically was frank basal cell epithelioma. Krompecher's concept of a basal cell origin for a basal cell cancer is generally accepted. There is a predilection for involvement of the forehead and nose and inner aspects of the cheek in both malignant and benign types of basal cell epithelioma. McDonagh called attention to the fact that many mammals, especially deer, have specialized hairs in the orbital facial fold, and explained basal-cell epithelioma on the basis of the lack of need of things that are present in the lower animals, and on the basis of hereditary cell rests. Glasunow expressed the opinion that basal-cell epithelioma on the face commenced in and about the lines of fusion of the embryonic facial processes. Paljtschewsky emphasized that basal-cell growths appear in areas which are well supplied with sebaceous glands and often

arise from comedones or nevi. Mallory has always championed a hair matrix origin for all types of basal-cell epithelioma. Neither in benign nor in malignant types of basal-cell epithelioma have I been able to demonstrate origin from the hair matrix cells. In the benign types, origin from the outer sheath of the outer hair follicles is frequently demonstrable and therefore one may speak of tricho-epithelioma or multiple benign cystic epithelioma. The ordinary basal cell cancer (basal cell in crypts), on the other hand, shows multiple points of origin from the basal cells of the epidermis. The same may be true in some instances of multiple benign cystic epithelioma and even is applicable to cylindromas.

DR. HERMAN GOODMAN, New York: It is conceded that the single layer of fetal ectoderm becomes the basal layer cells, which in turn, through chemical and physical changes, pass through the phases of squamous cells and corneum cells. The variations of the primary ectodermal layer become hair follicles, and so on. In facial blemishes, we have record of no less than thirty-seven supposed different types of lesions which arise from the ectodermal layer. Facial skin blemishes, for the greater part, are harmless clinically. Thousands of people receive treatment at the hands of barbers, beauticians and cosmetologists for facial skin blemishes. Rarely, if ever, is an ill effect reported. It becomes confusing, therefore, to have the terminology of skin cancer or cancer applied as a symptom or as a word in the same paragraph as epithelioma when it is utilized for benign cystic epithelioma. This presentation is the beginning of an orderly manner of continuing our studies in dermatology.

DR. DAVID BLOOM, New York: With regard to the question of heredity and family investigation, the paper by Dr. Goldman gives a hint of the value of this method. Of course, the study of one family tree in regard to a disease does not give exact information. But the study of many families with the disease and, particularly, twin studies may bring out facts which no other method of investigation has brought out until now. In dermatology there are a great number of problems which wait solution and which will probably not be solved unless newer methods of investigation are employed. I believe that cultivation of genetics in dermatology will contribute to the solution of many unsolved problems as to the etiology of disease.

DR. RICHARD L. SUTTON JR., Kansas City, Mo.: One must not be too certain of the benignancy of benign cystic epithelioma. In two cases that I have seen each of the many little tumors after having persisted for a long time in a harmless state has grown, producing a slowly progressive lesion, waxy, translucent, of hazelnut size, making a curious and typical picture. The face is grossly distorted, almost as if by nodular lepromas, with eventual ulceration. Such cases with thirty or forty progressive basal cell carcinomas at one time are difficult therapeutic problems. I have seen cases in which a lesion arching over the ear like a linear nevus, preauricular and extending upward, consisting of these little waxy pimples, took on active growth. One removes a mass of skin, including what one thinks is all of the tumor-bearing tissue; a year or two later at the upper end of the scar one removes a recurrence, and shortly one does the same thing still farther up the side of the head. Carefully questioned, practically all patients who have basal-cell carcinomas will tell, if they are observant, that the lesion began with a tiny, waxy pimple, which they thought was a blackhead and which they squeezed. Thereafter it grew. The question arises then whether their squeezing this lesion (which I presume was an epithelioma adenoides cysticum—it answers the description accurately) whether trauma changed the cell type; or did it simply translocate cells which were already potentially malignant and place them into more favorable environmental surroundings where they could grow? I think malignancy involves time considerations and that it is not possible to detect it solely by microscopic study of dead tissue. It is the prerogative only of the clinician to recognize malignant behavior, and the pathologist's original percept of whether a lesion is benign or malignant is accomplished by clinical observation. Malignancy is not a morphologic state. Many a lesion that microscopically looks

malignant isn't. Some that seem to be benign prove eventually not to be. It is only with the passage of time and as a lesion changes that one can know whether it is malignant or not.

DR. HYMAN J. GOLDMAN, St. Louis: With regard to Dr. Bloom's remarks about studying the heredity, he is right. We were inconvenienced somewhat by not being able to check up on many members of the family who could not be reached, some of them by reason of having been dead for many years. Dr. Sutton's remarks are applicable. The possibility of malignant degeneration has been discussed for many years and no definite conclusions reached. Of course, his remarks about a waxy pimple having finally turned into cancer, the waxy pimple being the description of the patient, are answered somewhat by S. Beck in his article in the Jadassohn handbook, in which he says that the only conclusive diagnosis in regard to multiple benign cystic epithelioma is the histologic one.

PRIMARY LESIONS OF THE JEJUNUM

DONOVAN C. BROWNE, M.D.
AND
GORDON McHARDY, M.D.
NEW ORLEANS

In 150,952 privately studied hospital admissions at Touro Infirmary (1926-1939) including 1,810 autopsies and 1,010,711 (1906-1939) cases at Charity Hospital of New Orleans with 6,160 (1936-1939) postmortem observations, primary pathologic changes of the jejunum were illustrated in a single instance each of traumatic regional enteritis and of intussusception, sixteen cases of diverticula, four perforated ulcers and eleven neoplastic involvements, of which seven were benign and four malignant.

This survey indicates an almost inconceivably low incidence. Yet the publications of recent years show increased cognizance of lesions of the small intestine. The number of case reports suggests either an increased incidence, the trend to report unusual pathologic conditions or diagnostic acumen. A study of the individual cases, however, reveals that only obvious lesions have been diagnosed by the clinician and roentgenologist. In many instances the establishment of the diagnosis came as a surprise to the exploring surgeon; most awaited necropsy study.

A proper concept of the anatomy and physiology of the jejunum coupled with an adequate evaluation of symptoms may increase the incidence of clinical diagnoses.

A review of reported symptomatology indicates three pertinent manifestations:

1. Pain is periumbilical or to the left and below the umbilicus, less frequently epigastric. Related to the site of the lesion it occurs at intervals after meals; the most proximal lesions cause almost immediate pain. The severity varies from quantitative discomfort in partially obstructive lesions to sharp pain when there is ulceration.

2. Obstruction is generally held to be an "all or none" phenomenon for jejunal lesions. This is inevitably so in primary intussusception and frequently so in neoplasms, especially the polypoid type, which produce intussusception in from 23 to 30 per cent of cases.

Because of lack of space, this article is abbreviated in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

From the Department of Medicine, Tulane University of Louisiana School of Medicine, the Department of Gastroenterology, Touro Infirmary, and the Charity Hospital.

This is perhaps the earliest, most frequent and most diagnostic manifestation of a jejunal neoplasm. However, jejunitis in its degrees, ulceration, diverticulosis with associated inflammation and encroaching neoplasms may produce intermittent mild and progressive blockage, depending on the mechanical nature of the pathologic condition.

3. Inanition and anemia, due to physiologic and mechanical derangement rendering nutritional absorption defective or the result of chronic blood loss, is prominent in the protracted case.

In an effort to strengthen our diagnostic armamentarium roentgenologists Pendergrass,¹ Cole,² Chamberlain³ and others have made stimulating investigations on the small intestine. Reviewing radiologic failures with the present routine (fluoroscopy, immediate and six hour films) one finds the accuracy in proved instances to be less than 50 per cent for jejunal neoplasms and



Fig. 1.—Jejunal delineation with barium sulfate enteroclysis.

10 per cent for jejunal diverticula; studies are negligibly positive in primary jejunal ulcers and jejunitis. Various types and thicknesses of contrast medium have been used. Miller-Abbott⁴ intubation studies and barium sulfate enteroclysis suggested by Gershon-Cohen and Shay have resulted in excellent physiologic, chemical and radiographic observations. The incidence of jejunal pathologic changes does not warrant the adoption of any of the thorough methods of roentgenologic investigation of the jejunum as a routine; this would be too costly and too time consuming. Two and four hour films taken as a routine have not proved of value. The radiologist therefore awaits the internist's alertness to request studies when indicated. When the need

1. Pendergrass, E. P.: The Small Intestine, J. A. M. A. **107**: 1859-1861 (Dec. 5) 1936.

2. Cole, L. G., and Pound, R. E.: Radiology **27**: 330-338 (Sept.) 1936.

3. Chamberlain, G. W.: The Roentgen Anatomy of the Small Intestine, J. A. M. A. **113**: 1537 (Oct. 21) 1939.

4. Miller, T. G., and Abbott, W. O.: Am. J. M. Sc. **187**: 595 (May) 1934.

arises it seems likely that intubation and barium sulfate enteroclysis offer a more satisfactory mucosal delineation both as to time and as to completeness of examination, than any other method.

This presentation covers pathologic conditions which are truly primary to the jejunum, with omission of congenital defects. Bovine tuberculosis may occur primarily in the gastrointestinal tract, but necropsy studies have not shown even an isolated instance in which the jejunum was the primary site. Avitaminosis, by producing mucosal edema and motor and nerve derangement, may lead to secondary changes in the tract, producing roentgenologically distorted mucosal patterns, localized distentions and barium stagnation. Hypermotility of the small intestine is a frequent occurrence in association with instances of functional dyspepsia. Purely functional disorders, dilatation associated with migraine and other such vague entities are difficult to establish on a sound clinical basis.

INTUSSUSCEPTION

Intussusception in the jejunum represented only 0.9 per cent of 3,784 cases of intussusception reviewed by Freilich and Coe.⁵ While only 5 per cent of all intussusceptions occur in adults, the jejunal type is more common to adult life than to childhood and is usually

A study of the literature since Crohn's initial publication reveals more than 600 cases of regional ileitis but the surprising recording of only twenty instances of jejunal involvement. Wilensky⁹ has ably covered the subject of etiology and was unable to ascribe the pathology to any one original cause, and he therefore concluded that it is an attempted overproductive but unsuccessful healing of a nonspecific lesion.

Through extensive studies of regional enteritis a definite correlation of the clinical manifestations with the pathologic process through four stages of the disease seems established. These studies are applicable to jejunal involvement:

1. The first phase is a state of acute inflammation with a thickened red, leathery, edematous bowel showing slight serosal exudate. The clinical picture may be that of acute appendicitis with the exception that there may be accompanying diarrhea, poor localization of pain and higher febrile rise than is expected in uncomplicated acute appendicitis. Differential diagnosis without laparotomy is not possible and its establishment as an entity is the result of careful exploration at the time of an appendectomy on a patient whose appendix does not substantiate the preoperative diagnosis of acute appendicitis.

TABLE 1.—Thirty-Four Cases of Primary Pathologic Changes of the Jejunum

	Touro Infirmary	Charity Hospital	Method of Diagnosis			Symptomatology					Average Age	Sex	
			X-Ray	Surgery	Autopsy	Obstruction	Pain	Perforation	Anemia	None		Male	Female
Admissions studied.....	150,032	1,010,711											
Autopsies reviewed.....	1,810	6,160											
Intussusception.....	1	0	0	0	1	1	1	0	0	0	2	0	1
Regional jejunitis.....	0	1	0	1	0	1	1	0	1	0	21	1	0
Ulcer.....	2	2	0	2	2	0	4	4	4	0	20	3	1
Diverticulum.....	7	9	6	0	10	2	5	1	8	8	30	5	11
Benign neoplasm.....	5	2	0	0	7	2	0	0	2	5	53	5	2
Malignant growth.....	3	1	0	3	1	3	4	0	2	0	41	3	1

secondary to a neoplasm. Ryan and Morgan⁶ reported a case which they considered primary, but there had been a previous gastro-enterostomy, which probably was related to the accident. In childhood the jejunal type is extremely rare, usually occurs without demonstrable cause and is therefore properly termed primary jejunal intussusception. In Freilich and Coe's series there were only four instances in twenty-nine cases of jejunal intussusception. The pathology of acute intussusception is the same regardless of the type and location. Clinically there are the dramatic manifestations of severely painful high intestinal obstruction. A palpable abdominal mass and bloody mucoid defecation occur in 25 per cent. Immediate surgical correction is indicated.

JEJUNITIS (REGIONAL ENTERITIS INVOLVING THE JEJUNUM)

Localized inflammatory lesions of the small intestine designated as nonspecific granulomas or inflammatory tumors have long been known. Crohn⁷ reactivated interest in the entity with his 1932 publication in which he coined the term "terminal ileitis," attempting to differentiate on an anatomic basis what he then believed to be a disease state peculiar to that segment. Harris and his collaborators⁸ brought recognition to enteritis at higher levels, reporting an instance in which the same pathologic process was found in the jejunum.

We suggest conservatism at this stage, i. e. a diagnostic exploration. The pathologic process is expected to subside spontaneously. The lesion may progress to stages of chronicity, but still this premise is not adequate to indicate radical thought. The major corrective procedures (enterocolostomy, enterostomy, resection) carry a measurable risk, and recurrences in a normal segment may occur after wide resection. Time and statistics may change our present conclusions.

2. Subacute or chronic nonulcerative enteritis is a progressive state which may show periods of remission. Abdominal distress, mild diarrhea, slight febrile reactions, leukocytosis and melena have persisted. Roentgenologically there are segments showing smooth contour with uniform narrowing and spasm. This and subsequent states are surgical problems.

3. Chronic ulcerative enteritis shows additional manifestations of moderately severe anemia, obstruction and melena; there may be a palpable tumor. X-ray examination shows irregular outline and caliber, with some loss of flexibility and changes in the mucosal pattern simulating ulcerative colitis.

4. The hyperplastic stage is an advanced state of the pathologic process with apparent inanition and marked obstructive manifestations suggestive of the clinical appearance in far advanced ulcerative colitis. A radiographic study reveals obliteration of normal outlines, loss of flexibility, shortening contraction of the lumen with stenosis and occasionally fistula formation.

5. Freilich, E. B., and Coe, G. C.: *Ann Surg.* 105:183 (Feb.) 1937.

6. Ryan, T. F. J., and Morgan, W. P.: *Brit. M. J.* 1:613 (March 25) 1939.

7. Crohn, B. B.: *Am. J. Digest. Dis. & Nutrition* 1:97 (April) 1934.

8. Harris, F. I.; Bell, G. H., and Brunn, H.: *Surg., Gynec. & Obst.* 57:637 (Nov.) 1933.

9. Wilensky, A. O.: *Surgery* 6:288 (Aug.) 1939.

There is a tendency to reason in the treatment of enteritis of the jejunum as one does in that of ulcerative colitis, i. e., to reserve radical surgery for the rapidly progressive instances which do not respond to every effort at conservatism but to act before the damage is too far advanced to expect results.

Regional enteritis manifest subsequent to severe abdominal trauma has been reported by H. E. Mock¹⁰ in three cases and by Bargen and his associates¹¹ at Mayo Clinic in two. In symptomatology, surgical aspects and pathology the lesions were those of regional enteritis. A single instance of such a coincidental jejunitis was encountered in our review of cases at Charity Hospital, and an abstract is included at the end of the paper.

DIVERTICULUM IN THE JEJUNUM

Diverticula in the jejunum, while still anatomic curiosities, are statistically the most prevalent primary jejunal lesions. Roentgenologically, Case¹² records the incidence to be 0.1 per cent; at autopsy instances are encountered in about 0.5 per cent of cases, according to a Johns Hopkins review. The cases are classified as congenital when the sac is made up of the same layers as the normal jejunal wall. Acquired herniations of the mucosa through the muscle layer are covered only by serosa. They are subject to inflammatory changes of diverticulitis and rarely perforate.

Etiologically they seem to be a product of degenerative changes, the greatest number being demonstrated in advancing age. The anatomic defect at the site of penetration of the blood vessels into the intestinal wall near the mesenteric attachment results in a point of decreased resistance which is subjected to irregular intestinal contractions that increase the intra-intestinal pressure. Charles Mayo¹³ observed a diverticulum form, during an intestinal operation, while the proximal bowel segment was in a state of contraction. The acquired diverticulum may be due to traction of some neighboring inflammatory process, as is contended by Fletcher and Castlenden. Multiplicity is characteristic.

Jejunal diverticula are considered innocuous; careful study of 100 cases reveals related symptoms in 35 per cent. Postprandial epigastric or left hypochondriac pain, flatulence, heartburn, occasional mild obstruction and melena have been accredited to their presence. By disturbance of function of the small bowel they may produce vitaminotic and nutritional deficiencies. Diverticulitis is infrequent because of the liquid contents and the free communication between the sac and the intestinal lumen. Perforation is rare. Watson¹⁴ reported jejunal obstruction caused by the weighty traction of an enterolith in a diverticulum.

Roentgenology offers the only preneecropsy method of diagnosis aside from surgery. Rankin and Martin,¹⁵ in reviewing 100 surgically proved cases found an x-ray diagnosis in only 10 per cent, substantiating the contention that jejunal diverticula are more often diagnosed during operation than by radiography.

Therapeutically, surgery is the only corrective measure available. Medically, dietary restriction and

measures aimed at avoidance of increased intra-intestinal pressure are offered. In the absence of clinical symptoms their removal is not justified. The severity of symptoms and the occurrence of complications indicate the need for surgical intervention. Resection, simple excision or a side tracking anastomosis are operative offerings.

CASE 1.—J. T. T., a white woman aged 69, was first seen at the age of 50 with discomfort in the lower part of the abdomen associated with constipation. Gastrointestinal studies then showed evidence of ileocecal adhesions (postappendectomy) with barium sulfate not yet in the cecum in the six hour film. When reexamined at the age of 60, free from gastrointestinal symptoms, a check gastrointestinal series showed, in addition, a single duodenal diverticulum. In 1939 she returned complaining of periumbilical pain about an hour after meals, waking her from sleep in the early morning. There were associated progressive asthenia, a slight loss of weight, anemia and mild hypovitaminosis. The patient was anemic and of small asthenic proportions, with skin and mucous membrane signs of vitamin deficiency. A radiographic study at this time revealed a single duodenal diverticulum and two diverticula in the jejunum.



Fig. 2.—Jejunal diverticulum.

A medical regimen consisting of a bland high caloric, high vitamin diet with frequent feedings and supplemental vitamins, aluminum hydroxide, sedatives and antispasmodics has not alleviated the symptoms.

This case reveals the development of diverticula in an aging patient who had a source of increased intra-intestinal pressure. The symptoms seem to be quite definitely related to the development of this pathologic picture. Operative correction seems to be the only recourse for relief, but the patient's aversion to surgery has delayed such therapy.

ULCER

Primary jejunal ulcer is a rarity. We have been able to find seventy-six reported instances since Rufz's initial publication on the subject in 1843. Apparently, this portion of the small intestine is resistant to ulceration. After gastro-enterostomy the jejunum loses its relative immunity, for marginal ulcers are frequently encountered. Our gastroscopic observations indicate that the majority of these occur in gastric mucosa at the anastomosis.

10. Mock, H. E.: *Surg., Gynec. & Obst.* 52: 672-689 (March) 1931.
11. Bargen, J. A.; Wisconsin M. J. 38: 877 (Oct.) 1939. Bargen, J. A., and Dixon, C. F.: *Proc. Staff Meets., Mayo Clin.* 10: 814 (Dec. 18) 1935. Bargen, J. A.: *M. Clin. North America* 12: 1573 (May) 1929.
12. Case, J. T.: *Diverticula of Small Intestine, Other Than Meckel's Diverticulum*, J. A. M. A. 75: 1463 (Nov. 27) 1920.
13. Mayo, C. H.: Personal communication to J. A. Bargen, Bargen, J. A.: *Rocky Mountain M. J.* 36: 537 (Aug.) 1939.
14. Watson, C. M.: *Surg., Gynec. & Obst.* 38: 67 (Jan.) 1924.
15. Rankin, F. W., and Martin, W. J.: *Ann. Surg.* 100: 1123 (Dec.) 1934.

In the limited study of primary jejunal lesions the etiology is even more obscure than in gastroduodenal ulceration. Theoretically, dystopic rests of the gastric mucosa may exist. The alkalinity of the jejunum is significant; gastric acidity could hardly be a factor in the development of an ulcer beyond the ligament of Treitz. Distant foci of infection, syphilis, tuberculosis, vasomotor phenomena and precedent jejunitis have an established position in the etiologic consideration. "Inherent predisposition" seems to have a place here as in the relation to the incidence of gastric and duodenal ulcers and leaves one with the conclusion that the cause of primary jejunal ulcer is unknown.

Pathologically the ulcer is a circular lesion varying from 4 mm. to 2 cm. in diameter; only 15 per cent are annular. Thickening, induration, stenosis and chronicity are prominent. The proximal portion of the jejunum is the portion of predilection, 72 per cent occupying such a site. All occur opposite the mesenteric attachment. A single ulcer is encountered in 80 per cent of cases, multiple ulcers are present in 18 per cent and associated gastric or duodenal lesions are expected in only 2 per cent. Some degree of penetration is usually present; in 82 per cent of the cases there was actual

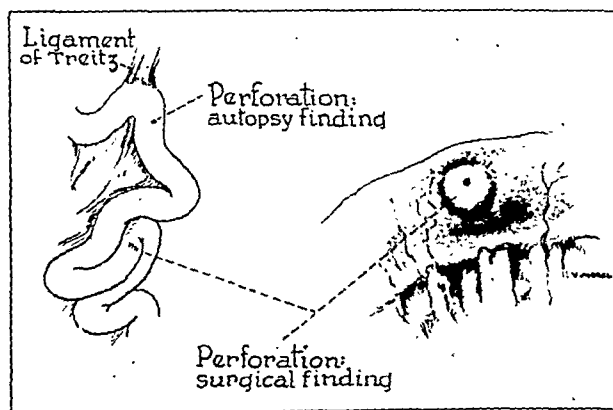


Fig. 3.—Jejunal ulcer.

perforation. Hemorrhage is recorded in 23 per cent of the cases and in all but six of these perforation also occurred. Microscopic examination revealed changes of chronic inflammation; no instance of malignant change was proved.

There is no clinical picture. Vague dyspeptic symptoms may bear slight resemblance to the "duodenal ulcer syndrome." Pain around the umbilicus or in the lower part of the abdomen is expected. If melena occurs one might expect the stool to be a cherry red. As with other pathologic changes in the small bowel, degrees of inanition and hypovitaminosis are prominent. Because of the fluid consistency of the jejunal contents, obstructive manifestations are not expected unless there is marked stenosis. Perforation results in an acute condition of the abdomen without specific localization.

Diagnosis is possible if the patient is available for radiographic study and there is sufficient suspicion to indicate delineation of the small bowel. A niche on the antemesenteric border of the jejunum with stasis proximal to the lesion is significant. A presurgical or antemortem diagnosis cannot otherwise be established.

Because of a statistical mortality of 60 per cent and the tendency to perforation, surgical intervention is the only logical therapy. There is no rationale for conservatism. Simple plication or radical resection is a matter of surgical judgment at the time of exploration.

CASE 2.—J. I., a white youth aged 19, was admitted, Nov. 23, 1939, with an acute condition within the abdomen of four days' duration. Five months previously he had attacks of colicky pain in the left inguinal region and mild postprandial discomfort in the upper part of the abdomen. An ambulatory regimen for ulcer gave no relief. In a three month interval he lost 25 pounds (11.3 Kg.). Two months prior to admission he experienced a three day period of diarrhea, profound weakness, umbilical pain and cherry red stools. This time his physician ordered a bed rest regimen for ulcer. From this time on he suffered almost constant pain in the left lower quadrant and had repeated episodes of emesis.

Four days before admission he experienced sudden severe pain in the left midsection of the abdomen which radiated to become periumbilical and later localized in the appendical area. There were associated emesis, a sharp febrile rise and a tendency to loose stools with progressive abdominal distention.

When examined the patient was acutely ill and febrile. The abdomen was distended symmetrically. There was acute tenderness in the right lower quadrant with poorly localized marked rigidity. One gained the impression of a thick edematous parietal peritoneum. No mass could be felt.

The leukocyte count was 22,000 with 93 per cent neutrophils. Flat and upright films of the abdomen were negative.

On the basis of these observations a diagnosis of a perforated hollow viscus was made, probably Meckel's diverticulum or appendix. The surgical consultant felt that the duration of the symptoms might well fit abdominal tuberculosis or Hodgkin's disease and advocated further observation.

The patient was treated conservatively with transfusions, Wangenstein suction, parenteral fluids, vitamins and alcohol. The Wassermann reaction, tests for agglutination and blood and stool cultures were repeatedly negative. Gastric analysis showed 21 units of free hydrochloric acid. The patient's condition became progressively worse with inanition and hypoproteinemia (serum proteins totaled 4.25 mg. per hundred cubic centimeters). Later he exhibited definite ileus despite from five to seven watery stools daily. Confirmatory x-ray examination also revealed free air and fluid intraperitoneally. Exploratory laparotomy revealed a perforated jejunal ulcer 24 inches beyond the ligament of Treitz. This was plicated.

On the second postoperative day pulmonary and renal infarcts developed and the patient died.

Autopsy revealed, in addition to generalized peritonitis, pulmonary and renal infarcts and the sutured jejunal ulcer another perforated jejunal ulcer 3 inches beyond the ligament of Treitz, which was oblong and measured 2 by 1 cm. Microscopic sections revealed only chronic inflammatory changes.

We cannot elicit any etiologic hint from this study. It is well illustrated that in this case a conservative medical regimen for ulcer was of no benefit. Earlier surgical intervention might have been of value.

NEOPLASM

Neoplasms primarily involving the jejunum are not as infrequently encountered as is generally thought. The actual number of cases diagnosed cannot be accurately determined, since tumors of the three divisions of the small intestine are summarily dealt with in autopsy and operative statistics. We reviewed 485 malignant and 170 benign lesions of the jejunum.

These new growths may be benign or malignant. It is confusing that carcinoids fall under both classifications. Their relative incidence is indicated by Raiford's¹⁶ investigation of 11,000 autopsies and 45,000 surgical specimens revealing eighty-eight tumors of the small bowel, of which fifty were benign and thirty-eight malignant. Our statistical study, however, shows that malignant lesions were more frequent than the benign type. Adenoma is the commonest benign tumor, carcinoma the most frequently encountered malignant growth.

16. Raiford, T. S.: *Radiology* 16: 253 (Feb.) 1931; *Am. J. Cancer* 18: 803 (Aug.) 1933; *Arch. Surg.* 25: 122 (July) 1932.

Etiologically it is postulated that the fluid alkaline contents with the absence of stasis explains the infrequency of malignant growths. There is no report of a chronic ulcer undergoing neoplastic change. That changes in Brunner's glands and in aberrant gastric and pancreatic tissue are etiologic factors is insignificant and, further, lacks substantiation.

Predilection does not favor the jejunum in the occurrence of neoplasms of the small bowel. An analysis of

TABLE 2.—*Malignant Tumors (485 Cases Reviewed)*

Carcinoma.....	234
A. Lymphosarcoma.....	69
B. Leiomyosarcoma.....	42
Sarcoma.....	20
C. Fibrosarcoma.....	8
D. Neurofibrosarcoma.....	3
E. Melanosarcoma.....	6
Malignant carcinoid.....	2
Chorionepithelioma.....	2
Malignant lymphoma.....	1

134 cases shows the duodenum predominating with fifty-one, the ileum next with forty-four and the jejunum next with thirty-nine instances.

The clinical picture is essentially the same for all neoplasms. Their differentiation is solely on a histologic basis. Flatulence, malaise, postprandial pain relieved by vomiting, asthenia and loss of weight and progressive anemia are the indefinite manifestations which occur in various degrees and combinations to precede obstruction which may be partial, recurrent, progressive or acutely complete. In adult life a neoplasm of the small bowel is the most frequent cause of intussusception. Each type of lesion has been reported as a cause, the polypoid type, of course, being the more frequent offender.

The nonoperative establishment of a jejunal neoplasm is difficult. Typical radiographic signs would be (1) dilatation of the proximal portion of the bowel with abnormal barium sulfate retention, (2) jejunal filling defect, (3) point of intestinal obstruction, (4) a dense shadow.

Surgical resection is the only curative method of management, whether the lesion is benign or malignant, for the former are certainly malignant by position and potentiality. When resection is not possible a short circuiting entero-enterostomy is the only alternative. High voltage roentgen therapy has a position of doubtful value.

Carcinoma primary to the jejunum is well established in 234 instances appearing in the literature. The relative incidence is illustrated by eight jejunal carcinomas reported from the Mayo Clinic as compared to 2,513 gastric and 2,767 rectal involvements.

The most common carcinomatous lesion is a polypoid stenosing type in favor over the annular ulcerating growths 3:1. The intestinal wall is not deeply involved until late, so that perforation is rare. It is significant that metastases are found in only 35 per cent of cases at the time of operation.

Sarcoma occurs in the small intestine more frequently than in the large bowel segments by a ratio of 2:1, as shown in Ullman and Abeshouse's¹⁷ review. The ileum is supposedly more often involved than the jejunum because of the greater amount of lymphoid tissue in this segment. Aneurysmal dilatation is a prominent occurrence related to either muscularis infiltration or to nerve plexus destruction. Sarcomatous lesions include lymphosarcoma, leiomyosarcoma, fibrosarcoma, neuro-

fibrosarcoma and melanosarcoma in relative frequency as listed.

Lymphosarcoma of the jejunum was found in sixty-nine cases. Starting in the lymphoid follicles, the wall is infiltrated, ulceration is characteristic and perforation results in 14 per cent of cases. Stenosis is rare, not occurring unless there is a considerable resultant fibrosis.

Leiomyosarcomas form a group of forty-two reported instances. They occur as circumscribed projecting oval tumors in half the cases and as an infiltrating mass in the other half. Showing a tendency to grow outward to the mesentery, they seldom cause obstruction.

Fibrosarcomas in twenty reports were either circumscribed or bulging with central necrosis and ulceration. As the entire wall is involved, stenosis is frequent.

Neurofibrosarcoma occurring as a primary jejunal lesion in eight cases presented no characteristic manifestation.

Melanosarcoma has been reported in three instances of jejunal involvement.

Malignant carcinoids or argentaffin tumors in the jejunum consist of nine instances found in 238 cases of involvement of the small bowel reported since Abernethy in 1907 differentiated these neoplasms from carcinoma. Their benignancy stressed by Forbus is disproved by more recent studies revealing metastases in 25 per cent of cases. Occurring as small submucosal nodules, they may bulge into the lumen as polypoid projections or may assume an annular form with fibrotic reaction.

Soresi¹⁸ and Sears¹⁹ each reported an instance of primary chorionepithelioma.

Cabot case 25242²⁰ was a malignant lymphoma of the jejunum.

Benignancy of jejunal lesions is only a histologic state and as such, aside from lipomas and enterocysts, is probably only a temporary condition. The occurrence of lipomas and enterocysts in the jejunum represents 25 per cent of benign tumors of the small bowel. Table 3 shows the relative frequency of benign tumors in 170 cases.

Variations between tumor types have been classified under the most closely related cell derivation. Multiplicity is common for hemangiomas and carcinoids; the other benign tumors more commonly occur singly. Their derivation is histologically apparent except for the enterocysts. Enterocysts may be the result of

TABLE 3.—*Benign Tumors (170 Cases Reviewed)*

Tumor	Cases	Tumor	Cases
Adenoma.....	75	Carcinoids.....	15
Fibroma.....	61	Lipoma.....	12
Myoma.....	34	Enterocysts.....	10
Hemangioma.....	16	Embryonic rests.....	3

* Variations between myoma and fibroma are classified under the latter.

† Endotheliomas have been included under hemangiomas.

pinched off diverticula or detached epithelium from the embryonic intestine. They consist of an epithelial mucosa, a thin connective tissue submucosa and a muscularis of two layers. The content is a pale clear albuminous alkaline fluid. Occurring in the submucosa, muscularis, subperitoneal region and mesentery, they may occasion volvulus, intussusception and stenosis.

18. Soresi, A. L.: *Am. J. Cancer* 28: 583 (Nov.) 1936.

19. Sears, J. B.: *Ann. Surg.* 97: 110 (June) 1933.

20. Cabot Case 25242, *New England J. Med.* 220: 1008 (June 22) 1939.

17. Ullman, Alfred, and Abeshouse, B. S.: *Ann. Surg.* 95: 878 (June) 1932.

Enucleation, resection, marsupialization and evacuation have been employed in their management, with the former two claiming more rationale.

CASE 3.—W. A. I., a white man aged 69, first seen Jan. 3, 1940, complained of postprandial periumbilical pain spontaneously relieved within a half hour. There were three occasions of emesis. He had lost 15 pounds (6.8 Kg.). A diagnostic survey, although not positive, suggested a lesion in the upper part of the gastrointestinal tract, and exploratory laparotomy was advised. The patient refused and was not seen again until March 16. In the interval he lost an additional 21 pounds (9.5 Kg.), and an exploratory examination was again advised. On the day of hospitalization the patient experienced melena for the first time.

Examination revealed evidence of inanition. There was a questionable movable mass in the left upper quadrant.

Gastric analysis showed hyperchlorhydria. There was marked hypochromic anemia and mild hypoproteinemia. Stools showed occult blood.



Fig. 4.—Jejunal lymphosarcoma (courtesy of Dr. Jerome Levy).

X-ray examination of the gastrointestinal tract revealed a wide sweeping curve of the duodenum with dilatation of the duodenum and proximal portion of the jejunum, barium sulfate retention and jejunal ulceration.

After adequate preparation an exploratory laparotomy was done revealing the proximal 30 cm. of jejunum enlarged and thickened, followed by an area of marked thinning studded with multiple nodules and perforated at one site. Jejunal resection, pyloric occlusion and gastrojejunostomy were successfully done.²¹

COMMENT

We present this review to bring attention to the importance of pathologic changes of the small bowel. Concentration of our study to the jejunum was stimulated by the fact that it is least often considered in a gastrointestinal survey. In our thirty-four case reports there is an indication that the more thorough study accorded the private patient increases the incidence in the private group.

21. Dr. Jerome Levy gave the authors permission to report his case illustrating a primary lymphosarcoma.

CONCLUSIONS

1. Primary pathologic lesions of the jejunum are relatively rare in contrast with other gastrointestinal lesions.

2. Clinical and roentgenologic diagnoses are infrequent; surgery and necropsy have revealed most of the instances that have been recorded.

3. Diagnosis is available by special radiographic technic, preferably enteroclysis, but such is not a practical routine procedure.

4. The clinician must become sufficiently aware of the entity to suspect its presence and request diagnostic x-ray examination.

ADDITIONAL ABSTRACTS OF CASES JEJUNITIS

CASE 4.—A Negro youth aged 21 seven days subsequent to severe abdominal trauma experienced umbilical and left lower quadrant cramping pain followed by quantitative dyspepsia and a severe sharp pain relieved by vomiting. There was mild diarrhea, melena and low grade fever. X-ray examination showed distention of the proximal portion of the jejunum. Exploratory laparotomy revealed a distended proximal portion of the jejunum with a thickened, acutely inflamed area in the midportion of the jejunum. A successful resection was done. The pathologic report was as follows: Six inches of jejunum had an acutely and markedly congested serosal surface. The thickened leathery wall showed acute exudative and chronic inflammatory changes. The lumen was constricted to 4 mm.

DIVERTICULA

CASE 5.—A Negro man aged 69 who had an acute condition within the abdomen and high intestinal obstruction refused surgery and died within four days. Necropsy revealed acute diverticulitis with perforation of a diverticulum 4 cm. beyond the duodenojejunal flexure.

CASE 6.—A white woman aged 36 complained of periumbilical pain and vomiting. X-ray examination showed barium sulfate stasis in the lower part of the jejunum with narrowing. Surgery revealed multiple diverticula in the lower jejunal segment; resection was successful.

JEJUNAL ULCERS

CASE 20.—A white man aged 58 complained of an acute condition within the abdomen of five hours' duration. Previous symptoms were suggestive of duodenal ulcer. The right lower quadrant was acutely tender. An exploratory operation revealed a perforated jejunal ulcer 12 inches beyond the ligament of Treitz. Resection and jejunojejunostomy were successful. Pathologic changes included 6 inches of jejunum and a perforated ulcer with chronic proliferative inflammatory changes.

CASE 21.—A Negro girl aged 5 years was markedly anemic with an acute condition of the abdomen and persistent vomiting. Cutaneous ulceration was present. *Ascaris lumbricoides* was present in the stool. The Wassermann reaction was negative. Autopsy revealed multiple perforated jejunal ulcers (mid-portion) but no specific microscopic abnormalities.

BENIGN TUMORS

CASE 23.—A white man aged 74 had a sudden onset of high intestinal obstruction. Autopsy revealed a jejunal lipoma causing intussusception.

CASE 24.—A Negress aged 49 had a sudden onset of high intestinal obstruction believed due to previous surgery. Autopsy revealed a fibroma of the jejunum contributing to high intestinal obstruction and acute kinking due to adhesions.

MALIGNANT TUMORS

CASE 30.—A Negro aged 39 complained of periumbilical pain, obstructive symptoms, diarrhea and loss of weight. An exploratory operation revealed an adenocarcinoma of the proximal portion of the jejunum with metastases to the omentum and regional lymph nodes. A palliative gastrojejunostomy was successful.

CASE 31.—A white man aged 56 with umbilical pain of three months' duration, loss of weight, malaise and anemia suddenly

experienced obstructive manifestations. An exploratory operation showed a jejunal neoplasm—not resectable—enterostomy. At autopsy an adenocarcinoma with metastases was found in the proximal portion of the jejunum.

JEJUNAL INTUSSUSCEPTION

CASE 34.—A white girl aged 14½ months suddenly manifested pain, a distended abdomen and bloody diarrhea. Autopsy revealed intussusception of the jejunum (no anatomic or pathologic cause was demonstrable).

1534 Aline Street.

ABSTRACT OF DISCUSSION

DR. DAVID ADLERSBERG, New York: The paper of Drs. Browne and McHardy proves the increased interest of the gastro-enterologist in lesions of the small bowel and represents a valuable contribution to our knowledge. It is important to realize and emphasize that the jejunum is the site of more extensive enzymatic digestion and absorption than any other part of the digestive tract; thus, pathologic changes of the jejunum are likely to impair the processes of digestion and nutrition to a great extent. It has been also my experience that definite periumbilical pain should call attention to the possibility of a lesion of the small intestine. Intubation with the Miller-Abbott tube and careful fluoroscopic and roentgenographic examination are time-consuming procedures but of essential diagnostic importance. It is agreed that organic lesions of the jejunum such as intussusception, diverticulosis and diverticulitis, primary jejunal ulcer, granuloma of the jejunum (regional jejunitis) and neoplasms (carcinoid, carcinoma, sarcoma and lymphosarcoma) are rare diseases in comparison with other pathologic changes of the gastrointestinal tract. However, it is my belief that milder changes of the jejunum of an inflammatory origin or on the basis of nutritional deficiency are not as infrequent as generally thought. Let me give one example: On gastroscopic examination of patients with gastric resection or gastro-enterostomy, one is frequently struck by the inflammatory changes of the stoma in its gastric as well as in its jejunal portion. In some of these cases the visible jejunitis is more impressive and probably more responsible for the patient's symptoms than the gastritis. One even wonders whether the jejunitis is not a precursor of a marginal ulcer in these cases. In other instances jejunitis cannot be diagnosed by direct visualization, yet an exact history of the case and a careful fluoroscopic and roentgenographic examination of the small bowel will possibly permit an indirect diagnosis.

DR. MAURICE FELDMAN, Baltimore: The roentgen demonstration of jejunal pathologic changes is often confusing because of the technical difficulties encountered in isolating the segments of the jejunum. The same difficulty, however, also holds true in the clinical diagnosis, particularly in the early cases. The information one obtains in the roentgen investigation of the jejunum is almost always the result of late manifestations of the disease. There can be no question that early abnormalities are being overlooked in the vast majority of cases. In this I am in accord with the authors. I should like to emphasize that early roentgen manifestations of disease of the jejunum may be radiologically depicted by a careful painstaking study of the mucosa of the different segments during the transit of the barium sulfate meal. I should like to ask the authors whether they have compiled their data to determine at what stage, particularly in carcinoma, it was possible to demonstrate the condition by means of the roentgen rays.

DR. DONOVAN C. BROWNE, New Orleans: We are all familiar with the work of Dr. Adlersberg on inflammatory lesions of the small bowel and our observations here are in no way contradictory. It is conceivable that such pathologic conditions may occur and especially are they impressive when one sees the changes proctoscopically which may occur in the rectosigmoid following acute infections of the upper respiratory tract. At what stage can the diagnosis of carcinoma be made? It is regrettable that at the time of diagnosis 30 per cent gave evidence of metastases and inoperability, stressing the need for more careful study of the small intestine. Unfortunately, adequate follow-up has not been available.

STILBESTROL-INDUCED GYNECOMASTIA IN THE MALE

CHARLES WILLIAM DUNN, M.D.

PHILADELPHIA

The therapeutic action of stilbestrol in the human being is under investigation by the Council on Pharmacy and Chemistry of the American Medical Association. This case is reported as a contribution toward defining its effect on the human species.

One of the established biologic effects of the naturally occurring estrogens is their growth-stimulating action on certain tissues and organs, one of which is breast tissue. It has also been experimentally established that when estrogenic substance is administered in sufficient amounts it has an inhibitory effect on anterior pituitary lobe trophic functions, among which are the production of growth hormone and the gonadotropic factor. A limited amount of clinical evidence supports these experimental observations.

I¹ have induced gynecomastia in males by administering the natural estrogenic substance. The tissue was studied and reported on by Dr. Charles F. Geschickter.² The production of breast development in the female by the administration of natural estrogenic substance has been reported by myself¹ and others. Premature breast development occurred in a girl aged 6 years with gonorrheal vaginitis treated with stilbestrol. Neither hypodermic nor suppository estrogenic therapy could be administered because of the child's physical resistance to these forms of treatment. The child was given 3 drops of stilbestrol solution (1 mg. per cubic centimeter) daily. After six weeks of stilbestrol therapy a mass approximately 2.5 cm. in diameter and 1 cm. in thickness appeared beneath the nipple in both breasts. At this period of therapy the vaginal discharge had disappeared.

I have observed marked breast development in young primary amenorrheal women treated with 5 mg. of stilbestrol daily for from fifty to sixty days. This is evidence that stilbestrol has a growth-promoting action on mammary tissue in the human female.

The present report concerns a male sexual criminal aged 27 years, now incarcerated, with a seven year history of repeated sexual offenses against minor females. Proper permission for the therapeutic experiment was obtained. The initial therapeutic objective in this case was to depress, if possible, the excessive and criminally directed sexual activity of the patient. That the excessive sexual activity was not the result of an increased activity of the so-called central nervous sexual center was indicated by the abnormally high urinary secretion of testis hormone and the gonadotropic factor. The assay report of his urine was 285 bird units of androsterone, 300 rat units of androsterone, 20 rat units of estrogen and 120 rat units of the gonadotropic principle of the urine of pregnant women or of placenta. The abnormally large penis and oversize testes, the sexual history and the hormone assay therefore indicated an anterior pituitary gonadotropic hyperactivity and a resultant increased activity of the testes and production of male hormone.

From the University of Pennsylvania Graduate School of Medicine.
1. Dunn, C. W.: Hormonic Induction of Menstruation in Amenorrheas of from Three Months' to Nine Years' Duration, *Am. J. Obst. & Gynec.* 30: 186 (Aug.) 1935.

2. Geschickter, C. F.: Breast Pathology in Relation to Endocrine Disorders in Piersol, G. M., and Bortz, E. L.: *Cyclopedia of Medicine, Surgery and Specialties*, Philadelphia, F. A. Davis Company, 1939, vol. 9, p. 549.

The patient was given orally 5 mg. of stilbestrol daily, beginning on June 20, 1940 and continuing for a period of sixty days, until a total of 300 mg. had been administered. Because a favorable and desired effect of therapy was obtained, 5 mg. of stilbestrol was then orally administered every other day for a period of thirty-six days. A total of 480 mg. of stilbestrol had been orally administered in a period of ninety-six days without evidence of toxic effect.

At the end of seventy-five days' therapy, when a total of 425 mg. of stilbestrol had been administered, the patient began to have sensitiveness in both nipples and observed a small lump beneath each nipple. During the subsequent twenty-one days the mass beneath the nipple increased progressively in size and sensitiveness and had become painful when he lay on the breasts.

The patient was examined at the end of ninety-six days of therapy, when a total of 480 mg. of stilbestrol had been administered. Physical examination revealed a hard, firm mass beneath the nipple of both breasts, the diameter of which was approximately 6 cm. and its thickness was approximately 2.5 cm. The edge and superior surface of the mass was freely movable beneath the skin, and the mass was separable inferiorly from the pectoral fascia. The mass was regular in outline, well defined and sensitive on palpation. Prior to therapy the breast region had been normal. The physical features of the gynecomastia produced in this male corresponded in character to the breast development produced in the young female child and young adult females to whom stilbestrol was administered.

In my opinion the mammary gland development resulting from the administration of stilbestrol is harder, firmer and of a denser (fibrotic) type of structure. The naturally occurring estrogens produce a breast tissue growth having the physical characteristics of normal breast tissue; these normal breast tissue characteristics are not present in stilbestrol-induced mammary growth. Another important point of differentiation observed is that the stilbestrol-induced breast development resolves at a much more retarded rate than the natural estrogen-induced mammary growth.

A dissimilarity of action of stilbestrol and the follicular hormone in the production of fibroids in the guinea pig uterus has been reported by Lipschutz and Vargas,³ who state: "This tumorigenic action of stilbestrol is much greater than that of the natural hormones (estradiol and estrone) when equal quantities are compared. . . . The guinea pig uterus increases beyond the normal weight more rapidly with stilbestrol than with the free natural hormones. This is tentatively explained by an inability of the organism to inactivate stilbestrol so rapidly and effectively as estradiol and estrone."

The initial objective of the therapy in this case was to inhibit the hypersexual state. Under the administration of stilbestrol the penis and testes have diminished to approximately two thirds of the pretherapeutic size. The patient states that there is an absence of libido and that masturbation does not produce an ejaculation of seminal fluid.⁴ A complete report of the sexual aspect of the case will be reported after urinary bioassays and testicular biopsy have been performed. Stilbestrol therapy is being continued.

In view of the foregoing subjective and objective clinical observations, it can be reported that stilbestrol produces mammary tissue development to a stage of advanced gynecomastia in the male and also stimulates the growth of mammary tissue in the female. The physical characteristics of the breast tissue reaction of stilbestrol and the naturally occurring estrogenic substances are markedly dissimilar in that the stilbestrol-induced mammary tissue growth is harder, firmer and denser and its rate of resolution after the discontinuance of therapy is markedly retarded as compared with that resulting from the administration of the naturally occurring estrogenic substances.

CONCLUSION

The administration of 480 mg. of stilbestrol to a man aged 27 produced a marked bilateral gynecomastia, the physical characteristics of which were dissimilar to that observed in males treated with the natural estrogenic substances. This dissimilarity of effect was also observed in female patients.

A marked diminution of sexual function, from a hypersexual state to what is considered a hyposexual state, has been obtained.

It is assumed that the therapeutic effect has resulted directly from depression of the anterior pituitary gonadotropic function and indirectly from inhibition of male hormone production in the testes or primary depression of testicular hormone formation. No clinical evidence of other disturbances in anterior pituitary function has been observed.

The administration of 480 mg. of stilbestrol produced no signs of the toxic effects attributed to stilbestrol.

265 South Nineteenth Street.

ALLEGED HEPATOTOXIC ACTION OF STILBESTROL

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AND

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CHICAGO

Diethylstilbestrol, the synthetic estrogen which has been named stilbestrol for convenience, has aroused widespread interest because of its remarkable effectiveness in replacement therapy.¹ In addition to possessing most or all of the therapeutic properties of the natural estrogens, it has great potency on oral administration, which makes it a convenient substance to use.² However, there has been much concern over the significance of certain side effects which occur in some patients following stilbestrol medication.

Most authors have reported that about 10 to 20 per cent of their stilbestrol-treated patients complained of gastrointestinal distress, principally nausea.³ The reports

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4. Testicular biopsy of the right and left testis performed by Dr. Charles W. Charny revealed a generalized degenerative process. There is no evidence of normal cell growth and not a single tubule displays cellular development to the spermatid stage. The intertubular spaces appear to be edematous and contain a reduced number of interstitial cells.

correspond with our own experience. Shorr and his associates,⁴ on the other hand, have reported a far higher incidence of untoward reactions (approximately 80 per cent), which include skin eruptions, lassitude, headache and psychosis. The last-mentioned authors have also presented some admittedly inconclusive evi-

TABLE 1.—*Clinical Results with Stilbestrol Compared to Those Obtained with Estradiol in the Same Group of Menopausal Women*

Case Number	Estradiol, 400 Oral Rat Units Daily	Stilbestrol, 0.5-1.0 mg. Daily
1.....	0	0
2.....	0	++
3.....	0	++
4.....	0	+++
5.....	++	++
6.....	++	++
7.....	++	++
8.....	+++	+++
9.....	+++	+++
10.....	++++	++++
11.....	++++	++++
12.....	++++	++++

++++ indicates complete relief.

dence of liver damage in their stilbestrol-treated patients. Using the bilirubin retention and the hippuric acid excretion tests, they found some indication of decreased liver function by the first method but not by the second.

We report some observations on stilbestrol which, while they do not explain the minor unpleasant reactions which occur in some patients, lead us to believe that the drug is not significantly toxic to the liver.

METHODS AND RESULTS

Our patients were an unselected group of women suffering from the typical menopausal syndrome. In all but a few the menopause was of natural origin. Since the toxicity of a substance has little significance except in relation to its therapeutic dosage, our first work with stilbestrol was an attempt to approximate the latter. Table 1 summarizes our results in a representative group of patients of whom the same ones were treated at different times and after suitable control

TABLE 2.—*Bromsulphalein Retention in Stilbestrol-Treated Menopausal Women and in Untreated, Apparently Normal, Women in the Same Age Group*

Stilbestrol-Treated Group				Untreated Control Group			
Patient	Age, Years	Treatment		Bromsulphalein Retention, Percentage	Patient	Age, Years	Bromsulphalein Retention, Percentage
		Days	Mg.				
1. B. L.	36	30	20	10	1. S. S.	57	5
2. R. S.	51	42	46	10	2. I. T.	58	5
3. G. B.	50	168	53	10	3. B. W.	40	10
4. M. H.	47	28	48	15	4. N. L.	41	10
5. H. B.	45	90	82	15	5. L. C.	44	10
6. R. Lo.	49	93	90	15	6. S. P.	52	10
7. L. K.	42	168	112	15	7. S. M.	39	15
8. H. B.	45	122	122	15	8. S. S.	42	15
9. R. L.	41	196	146	15	9. R. K.	48	15
10. R. C.	55	70	42	30	10. M. M.	41	20
11. S. Se.	50	196	86	35	11. L. G.	44	20
12. L. D.	54	28	30	60	12. E. M.	57	25

periods with stilbestrol⁵ and estradiol respectively. The number of plus signs indicates our comprehensive judgment of the degree of relief obtained in each instance; 4 plus indicates complete relief of all signs and symp-

toms. It was our practice to start stilbestrol treatment with 0.5 mg. daily and to raise this dose to 1.0 mg. daily if complete relief was not obtained with the smaller dose. It may be seen that the oral administration of 0.5 to 1.0 mg. of stilbestrol daily yields somewhat better relief of the menopausal syndrome than does the daily ingestion of 400 oral rat units of estradiol.

In view of the age group in which our patients fell it seemed inadvisable to select one of the more highly sensitive tests of liver function, which would undoubtedly reveal minor degrees of asymptomatic liver damage in many of our patients whether they were treated with stilbestrol or not. We therefore chose the bromsulphalein retention test, which is generally recognized as being sensitive to liver deficiency of clinically significant degrees. As used by us, 5 mg. of the dye per kilogram of body weight is injected intravenously in one arm. One half hour later a blood sample is withdrawn from the opposite arm. The amount of bromsulphalein remaining in the serum at that time is determined colorimetrically. A retention of 15 per cent is considered to be the upper limit of normal.

Table 2 shows a comparison of the results of the bromsulphalein test in 12 menopausal women who had been treated with stilbestrol for various lengths of time, with the results in an equal number of apparently normal, untreated women in the same age group. Only 3 women in the group treated with stilbestrol

TABLE 3.—*Bromsulphalein Retention in the Same Menopausal Women, Before and After Treatment with Stilbestrol*

Patient	Age, Years	Treatment			Bromsulphalein Retention	
		Daily Dose, Mg.	Duration, Days	Total Dose, Mg.	Before Treatment, Percentage	After Treatment, Percentage
1. S. P.	46	1	21	21	10	10
2. L. C.	48	1	30	30	10	5
3. F. W.	38	1	40	40	10	10
4. S. S.	47	1	42	42	15	10
5. B. B.	47	1	147	147	15	15
6. C. W.	46	5	29	137	35	35
7. E. S.	45	5-10	23	130	40	30
8. A. F.	41	10	8	80	60	30

and an equal number in the untreated group showed abnormally high bromsulphalein retentions. Nor was there any relationship between the total dose of stilbestrol and the degree of dye retention. It is probable, therefore, that the indicated liver damage was present in the menopausal women before the treatment was instituted.

However, the somewhat greater degree of dye retention in the entire group of menopausal women as compared to the control women suggested the possibility that stilbestrol might have some injurious effect on livers which were already suffering from some slight damage. Bromsulphalein retention tests were therefore done on another group of menopausal women, both before and after they had received stilbestrol. It will be noted in table 3 that in not a single instance was the bromsulphalein retention greater after stilbestrol treatment than before it. In fact, the reverse was true in 4 out of the 8 cases so observed. This seems especially significant in view of the fact that patients 6, 7 and 8 manifested abnormally high degrees of dye retention before treatment and were purposely given 5 to 10 times our usual therapeutic dose of stilbestrol.

At this point in our work it was quite apparent that, as judged by the bromsulphalein retention test, therapeutic doses of stilbestrol did not cause liver damage, nor did they aggravate the preexisting mild deficiencies

4. Shorr, Ephraim; Robinson, F. H., and Papanicolaou, G. N.: A Clinical Study of the Synthetic Estrogen Stilbestrol, J. A. M. A. 113: 2312 (Dec. 23) 1939.

5. E. R. Squibb & Sons supplied the stilbestrol.

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present in some menopausal women. However, none of the women available for this study had manifested any significant clinical signs or symptoms of liver damage. It therefore seemed important to test the possible toxicity of stilbestrol in at least 1 patient (whether menopausal or not) with frank and unquestionable liver disease. The opportunity of a test soon presented itself in J. L., a white man aged 38 who was convalescing from an attack of acute hepatitis.

Before detailing the experimental procedure with the patient just mentioned it is necessary to outline certain animal experiments which, in addition to the observations already presented, had given us sufficient assurance that he would come to no harm.

TABLE 4.—Indexes of Liver Function in a Dog, Before and After Prolonged Administration of Stilbestrol (10 Mg. Daily for Sixty Days)

	Before 3	After 3
Icterus index.....	125	147
Serum cholesterol, mg. per 100 cc.	41	47
Total.....	84 (67.2%)	100 (68%)
Free.....	Less than 5%	Less than 5%
Esters.....	Less than 5%	Less than 5%
Bromsulphalein retention.....	71	50
Dextrose tolerance (blood sugar, mg. per 100 cc.)*	286	324
Control.....	145	121
30 minutes.....	63	61
60 minutes.....	65	26
90 minutes.....	74	51
120 minutes.....	75	
150 minutes.....		
180 minutes.....		

* 1.75 Gm. of dextrose per kilogram of body weight, injected intravenously in 30 per cent solution.

1. Twelve adult female rats were placed on our usual Purina Fox Chow diet supplemented with 10 per cent powdered milk. In this diet was mixed an amount of stilbestrol which, from the quantities of food eaten each day, resulted in a stilbestrol intake of about 7 mg. per rat daily. At the end of fourteen days the amount of stilbestrol in the diet was doubled, and the new amount was continued for another period of fourteen days. This dose of stilbestrol, when considered in terms of the body weight and life span of the rat, corresponds to a relatively enormous dose over a period of several years in man. Nevertheless the animals were grossly normal when killed for postmortem examinations. The livers and kidneys failed to show any gross or microscopic pathologic conditions, except for the occasional slight, cloudy swelling which frequently be observed in the tissues of normal rats.

2. To ascertain the cell structure of the liver and kidneys of stilbestrol on the absence of toxic effect on hepatic function, was paralleled by an experiment on a dog. This animal ingested a similar experiment was done on a dog. Table 4 gives the results of our estimations of the icterus index, serum cholesterol, dextrose tolerance and bromsulphalein retention, both before and after the stilbestrol treatment. There was no evidence of any functional impairment.

Patient J. L. entered the hospital complaining of nausea, vomiting, jaundice, pruritus and clay-colored stools, of three weeks' duration. On physical examination there was slight tenderness in the right upper quadrant of the abdomen. The liver was palpable 4 cm. below the costal margin in the right midclavicular line; the lower edge was smooth and firm. A diagnosis of acute catarrhal jaundice with hepatitis was made. The icterus index at the height of the patient's illness had reached a level of 80, his cholesterol-cholesterol ester ratio was reduced to 27 per cent. He had returned to normal and his cholesterol-cholesterol ester ratio was up to 59 per cent. His bromsulphalein

retention at this time was 60 per cent. His symptoms were entirely gone.

The daily administration of 10 mg. of stilbestrol orally was now begun and continued for three weeks. During this period, despite the intake of 210 mg. of the drug, the patient continued to show clinical improvement. By the end of the period the icterus index was still normal, the cholesterol-cholesterol ester ratio had become normal (78 per cent) and the bromsulphalein retention had dropped to 20 per cent.

SUMMARY

With the therapeutic doses (1 mg. daily) and the particular product which we used there was no evidence of any toxic action of stilbestrol on the livers of the menopausal women whom we treated. This was true even with doses of 5 to 10 mg. daily and in women who exhibited some liver dysfunction to begin with as judged by the bromsulphalein retention test. Furthermore, relatively huge doses of stilbestrol in rats and a dog did not give rise to gross or cellular pathologic conditions of liver or kidneys or to liver damage as judged by various criteria of hepatic function. Finally, a patient with indubitable liver damage who was recovering from an attack of acute hepatitis was able to take ten times our usual therapeutic dose of stilbestrol for a period of three weeks without the slightest evidence that his convalescence had been impeded.

It must be concluded that in our experience stilbestrol is not significantly toxic to the liver. We are unable to explain the gastrointestinal distress which follows the use of stilbestrol in some patients. Until this is explained it seems wise to discontinue the administration of stilbestrol in any patient who begins to complain of nausea or other side effects. Meanwhile, there seems to be little reason for withholding the use of a potent and convenient estrogen in such patients as do not experience these side effects.

CLINICAL STUDIES ON STILBESTROL

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In a previous paper¹ we have reported our results on animal experiments concerning the toxicity and activity of stilbestrol. We found that the close similarity of the action of natural and synthetic estrogenic substances on the female sex organs and the pituitary gland of immature, mature and castrated animals could be confirmed. Some evidence of toxicity could be observed in our animals after we administered doses of stilbestrol as low as 0.1 mg. three times a week, although the changes at higher dose levels were not as drastic and alarming as those reported by Loesser.² Clinically the drug has been used by numerous investigators of the Continent and recently also in the United States for

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1. von Haam, Emmerich; Hammel, M. A.; Rardin, T. E., and Schoene, R. H.: Experimental Studies on the Activity and Toxicity of Stilbestrol, to be published.
2. Loesser, Arnold: Untersuchungen über die Pharmakologie und Toxikologie synthetischer Brunststoffe (4, 4'-Dioxy-a, b-Diäthylstilben), Ztschr. f. d. ges. exper. Med. 105: 430, 1939.

the treatment of various ovarian disorders. While the reports on the activity of the drug in the majority of cases are very encouraging, considerable discrepancy exists with regard to the untoward symptoms observed in some patients after its administration. It is the latter fact which up to the present time has caused the American Medical Association to withhold official recognition of stilbestrol. In reporting our own clinical experiences with this drug we shall discuss separately our findings concerning its efficacy together with the pertinent data from the literature and our clinical investigations concerning the toxicity of this drug in human beings.

ESTROGENIC PROPERTIES OF STILBESTROL

First tested on a more extensive scale by Winterton and MacGregor,³ stilbestrol has proved highly effective in controlling symptoms of menopause. Three patients with kraurosis vulvae were markedly improved. Ten of 11 patients with secondary amenorrhea started to bleed after sufficient therapy. Tüscher⁴ treated successfully postpartum amenorrhea with 1.5 mg. once a week. If given to normal women it produced sensitive swelling of the breasts and clitoris with increased libido. Kellar and Sutherland⁵ used it for successful control of menopause, senile vaginitis, leukoplakia and secon-

TABLE 1.—Clinical Summary of Stilbestrol in the Treatment of the Menopause

	Series A	Series B
1. Total number of patients treated.....	58	67
Age		
Below 30.....	3	2
Between 30 and 40.....	19	9
Between 40 and 50.....	29	37
Over 50.....	7	19
Diagnosis		
Secondary amenorrhea.....	31	24
Postpartum amenorrhea.....	26	42
Menopausal symptoms.....	1	11
2. Form and duration of therapy		
Total doses		
1 to 20 mg.	24	48
20 to 50 mg.	26	15
50 to 100 mg.	8	3
Over 100 mg.	0	1
Single doses		
Oral (less than 1 mg.).....	30	33
Oral (more than 1 mg.).....	2	5
Parenteral (less than 1 mg.).....	5	4
Parenteral (more than 1 mg.).....	18	37
Duration		
Up to 1 month.....	17	35
1 to 2 months.....	23	25
Over 2 months.....	16	7
Total.....	2	0
3. Results		
Good: complete relief of all symptoms.....	18	48
Fair: partial relief of all symptoms.....	21	8
Poor: no or little relief.....	17	
Adverse: addition of toxic symptoms made patient feel worse than before.....	2	9
4. Comparison with other therapy		
Number of patients treated previously with other oestrogenic substances.....	22	59
F.....	7	25
E.....	4	17
F.....	11	12
5. Toxic symptoms after stilbestrol therapy		
Total number of patients.....	28	24
Headache.....	22	22
Nausea.....	0	2
Vomiting.....	12	3
Dizziness.....	4	10
Anorexia.....	2	3

dary abortion. Guldberg⁶ was able to produce a normal progestational endometrium by giving a 22 year old castrate woman with intact uterus 20 mg. of stilbestrol

for eighteen days followed by 30 rabbit units of synthetic progesterone for six days. Evelbauer⁷ reported success of treatment in 50 climacteric patients with comparatively small doses. He did not have any success treating uterine hypoplasia and amenorrhea and recommended the natural estrogen for patients with these conditions. Buschbeck and Hausknecht⁸ reported

TABLE 2.—The Effect of Stilbestrol on the Urinary Bioassay

	Number of Cases	Gonadotropic Excretion in 24 Hours			Theelol Excretion in 24 Hours		
		Over 50 Mouse Units	Trace	Negative	Over 100 Mouse Units	Trace	Negative
Before treatment.....	35	51%	26%	23%	3%	11%	86%
After treatment of at least 1 month.....	11	27%	9%	64%	55%	18%	27%

TABLE 3.—Survey of Toxic Symptoms Observed in the Literature

Author	Total Number of Cases	Number of Toxic Reactions	Percentage	Comment
Winterton and MacGregor	24	6	25	Nausea
Loesser.....	11	2	18	Nausea
Kellar and Sutherland.....	15 (?)	3	20	Transient nausea
Varangot.....	18	13	87	Late and early symptoms; 4 cases of absolute intolerance
Bishop et al.....	46	3	65	Nausea and headaches
Shorr et al.....	44	35	80	In 14 therapy had to be stopped
Kurzrok et al.....	40	26	65	In 10 therapy had to be stopped; nausea, malaise
MacBryde et al.....	37	8	22	Nausea and 3 cases of vomiting
Karnaky.....	189	Occasionally	..	Nausea
Geist and Salmon.....	38	8	21	Anorexia, dizziness, vomiting
Burton and Engle.....	17	1	6	

success in cases of amenorrhea with total doses of as little as 20 mg., given in 5 mg. doses. A similar experience was reported by Heisler.⁹ Engelhart¹⁰ induced "menstruation" in castrate women. Brühl¹¹ treated successfully endometrial hemorrhages with 2 to 3 mg. of stilbestrol. He also had success in the treatment of dysmenorrhea, dyspareunia and lack of libido. According to Lindemann¹² the estrus produced by diethylstilbestrol dipropionate lasted twice as long as the one produced by estradiol benzoate. Varangot¹³ found stilbestrol three times as effective as crystalline estrone if given by injection and six times as active as estradiol benzoate when given by mouth. In 18 cases improvement was achieved by daily doses of 0.3 mg. The danger of overdosage was stressed by Ehrhardt, Kramann and Schäfer.¹⁴ They found 12 mg. of stilbestrol

7. Evelbauer, K.: Zur Behandlung mit Stilbenpräparaten. München. med. Wchnschr. **86**: 1118, 1939.

8. Buschbeck, H., and Hausknecht, K.: Ueber die Wirkung von Stilboestrol beim Menschen. Klin. Wchnschr. **18**: 160, 1939.

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10. Engelhart, E.: Der Aufbau der Proliferationsschleimhaut bei der kastrierten Frau durch einen synthetischen oestrogenen Wirkstoff. Wien. klin. Wchnschr. **51**: 1356, 1938.

11. Brühl, R.: Erfahrungen mit der therapeutischen Anwendung der Cyrene synthetischer Präparate mit den Wirkungen des weiblichen Sexualhormons. München. med. Wchnschr. **86**: 582, 1939.

12. Lindemann, W.: Ueber Cyren—"Bayer"—und seine Wirkung auf die Milchsekretion und zur Laktationsbeeinflussung. Zentralbl. f. Gynäk. **63**: 719, 1939.

13. Varangot, M. J.: Activité oestrogène et toxicité du 4:4' dihydroxy a: b diethylstilbene (stilboestrol). Bull. Soc. gynéc. et d'obst. **28**: 160, 1939.

14. Ehrhardt, K., Kramann, H., and Schäfer, H.: Vorläufige klinische Ergebnisse mit östrogenen Stilben-Präparaten. München. med. Wchnschr. **86**: 261, 1939.

3. Winterton, W. R., and MacGregor, T. N.: Clinical Observations with Stilbestrol (Diethylstilbestrol). Brit. M. J. **1**: 10, 1939.
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5. Kellar, R. J., and Sutherland, J. K.: Clinical Experiences with a New Synthetic Estrogen—"Stilbestrol" (Diethyl-Stilbestrol). J. Obst. & Gynaec. Brit. Emp. **46**: 1, 1939.
6. Guldberg, Erik: Echte Menstruation bei einer kastrierten Frau nach Zufuhr von synthetische hergestellten Hormonstoffen. Zentralbl. f. Gynäk. **62**: 2584, 1938.

sufficient to produce a normal proliferating endometrium and recommended 0.5 to 1 mg. as single doses and 2 to 5 mg. as a weekly dose for the treatment of the menopause. Bishop, Boycott and Zuckerman¹⁵ produced withdrawal bleeding in 8 patients with amenorrhea and rhythmic hemorrhages in 2. Biopsy of the breast after administration of 280 mg. by mouth showed epithelial proliferation with no increased secretory activity. In their summary Bishop and his co-workers emphasized the close resemblance of the effect of stilbestrol to that of natural estrogen. Both produce withdrawal bleeding, a proliferative type of endometrium, growth of the hypoplastic uterus, relief of the menopausal syndrome, restoration of the vaginal smear into the estrous type, proliferation and activation of the mammary glands with painful swelling of the breasts and relief of dysmenorrheic pains. Cessation of lactation after administration of stilbestrol in cases of stillbirth was reported by Tietze¹⁶ and Lindemann.¹² Peel¹⁷ showed that stilbestrol had little value in inducing labor although it

plasia the therapeutic effect of stilbestrol was identical with the one produced by the natural estrogen. MacBryde, Freedman, Loeffel and Allen²⁰ studied 37 cases of various types of ovarian deficiency. They were able to produce withdrawal bleeding and mammary growth at will. Implantation of pellets weighing 100 mg. each to 6 castrated patients produced an estrous type of vaginal smear within two days and endometrial proliferation within seven days. The menopausal symptoms were greatly relieved as long as the pellets remained in place. The average daily absorption could be determined as ranging from 0.127 to 0.250 mg. Karnaky²¹ treated 189 patients with menstrual disorders. He found stilbestrol as effective as natural estrogens. Geist and Salmon²² used the drug in 38 menopausal women in doses of 1 to 5 mg. three times a week or in tablets of 3 to 5 mg. daily. The women showed a positive vaginal smear as early as four days after treatment and a complete control of hot flashes. However, headaches and nervousness were not strikingly relieved.

TABLE 4.—Effect of Stilbestrol on Blood of Six Patients

	Week	S. B. 16 mg. Severe nausea	T. S. 24 mg. Severe nausea	V. W. 24 mg. Sick twice; felt improved	L. H. 24 mg. Sick twice; good results	M. A. 24 mg. Some nausea; good results	C. T. 24 mg. No nausea; good results
Doses.....
Results.....
Red blood cells in millions per cubic millimeter	1 2 3 4	3.50 3.40 4.21 3.63	4.78 5.10 5.45 4.37	5.30 4.96 4.22 4.57	5.12 4.38 3.70 4.66	5.72 4.82 4.97 4.45	4.05 4.35 4.67 3.56
Hemoglobin in grams per hundred cubic centimeters	1 2 3 4	10.9 10.9 12.0 12.0	13.1 15.6 15.3 13.7	13.7 13.2 12.8 15.3	16.7 14.4 13.7 15.7	15.8 16.2 16.0 15.6	13.1 12.0 10.9 13.4
Percentage of reticulocytes.....	1 2 3 4	0.6 0.4 0.6 1.0	0.4 0.4 2.4 2.0	1.4 0.8 1.0 2.4	2.4 3.6 1.6 4.6	3.6 1.8 0.8 0.2	0.4 1.5 2.4 2.0
Leukocytes in thousands per cubic millimeter	1 2 3 4	5.85 4.85 5.30 3.73	10.20 9.45 12.00 10.40	7.30 7.80 7.40 6.80	9.65 9.10 10.20 5.75	8.60 7.85 7.35 6.52	8.80 10.15 9.00 5.67
Thrombocytes in hundred thousands per cubic millimeter	1 2 3 4	4.74 4.96 5.66 3.73	8.28 7.38 7.98 5.10	3.06 3.03 5.11 3.06	5.22 2.98 2.98 5.11	5.23 4.00 4.00 5.11	6.27 8.44 8.44 6.27

was definitely advantageous in increasing the tone and uterine contractions.

In the United States six reports have appeared up to the time this report was written on clinical trials with stilbestrol. Shorr, Robinson and Papanicolaou¹⁸ studied its effect on forty-four women, many of whom had been treated previously with natural estrogens, and confirmed its powerful estrogenic action. Only 2 of the 44 patients failed to show an estrous type of vaginal smear. They found that 1 mg. of stilbestrol was equivalent to 1.7 mg. of estrone and emphasized the great advantages of oral administration. Kurzrok and his co-workers¹⁹ studied 40 cases of various gynecologic disorders. Fifteen menopausal patients obtained symptomatic relief, sometimes as early as twelve hours after the initial treatment. In the other 25 cases of amenorrhea, oligomenorrhea, dysmenorrhea and uterine hypoplasia the therapeutic effect of stilbestrol was identical with the one produced by the natural estrogen.

In our clinical studies a series of 125 patients with surgical and natural menopause were treated from two weeks to six months with doses ranging up to 60 mg. (table 1). Series A is composed of patients studied at the endocrine clinic of the University Hospital; series B comprises patients treated in private practice. We thought a separation of our material into these two groups might be of interest since a marked difference existed between these patients with respect to the presentation of their symptoms and of any subsequent changes. The stilbestrol was administered in the majority of cases by oral therapy in daily doses of 0.2 to 0.5 mg. This was found to be the most effective type of treatment as it produced the least amount of disagreeable symptoms. Parenteral therapy was usually used in doses of 1 mg. twice a week. The duration of treatment extended in the majority of cases from one to three months. Only 2 patients had therapy for one year.

Our results showed a considerable difference between the patients of series A and B, justifying the division

15. Bishop, P. M. F.; Boycott, Muriel, and Zuckerman, S.: The Estrogenic Properties of "Stilbestrol" (Diethylstilbestrol), *Lancet* 1: 5, 1939.
 16. Tietze, K.: Zur Einführung des Cyrens in die Therapie hormonaler Störungen der weiblichen Genitalfunktion, *Geburtsk. u. Frauenh.* 1: 486, 1939.
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 18. Shorr, Ephraim; Robinson, F. H., and Papanicolaou, G. N.: A Clinical Study of the Synthetic Estrogen Stilbestrol, *J. A. M. A.* 113: 2312 (Dec. 23) 1939.
 19. Kurzrok, Raphael; Wilson, Leo, and Perloff, W. H.: The Action of Diethylstilbestrol in Gynecological Dysfunctions, *Endocrinology* 26: 581, 1940.

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 21. Karnaky, K. J.: Stilbestrol, the New Synthetic Estrogenic Hormone, *Urol. & Cutan. Rev.* 43: 633, 1939.
 22. Geist, S. H., and Salmon, U. J.: Indications for Estrogen Therapy, *New York State J. Med.* 39: 1759, 1939.

of our material. While 71 per cent of the patients of series B reported complete relief of all symptoms, only 30 per cent of our charity patients were content with the therapy. Poor or adverse results were obtained in only 13 per cent of the privately treated patients, while it was present in 32 per cent of the patients treated at the clinic. The reason for this marked discrepancy is probably a less careful selection of suitable material in series A, since the mental capacity of our patients often makes proper recognition of the menopausal syndrome difficult. Economic factors and social problems may also have some part in the differences in our therapeutic results. Eighty-one patients of both series had had previous experience with other estrogenic drugs. Thirty-two per cent of series A and 42 per cent of series B reported better results after stilbestrol than

as early or as consistently, and we wish to withhold further comment on this until more studies have been accomplished. Excessive stimulation of the sexual organs was found in a sufficient number to be worth mentioning. The most alarming symptom was the appearance of vaginal bleeding, which was noticed in 8 cases. It occurred in patients who at the time of treatment were one and a half years past the last men-

TABLE 5.—Laboratory Tests in Patients Treated with Stilbestrol

Laboratory Test	Normal Control	After Therapy
Icterus index.....	3-9	2-9
Prothrombin determination.....	80-90	85-100
Weltmann coagulation band.....	1-7	3-6
Serum bilirubin.....	0.2-1.5	0.2-0.2
Blood chlorides.....	462.9-519.8	346-519.8
Bromsulphalein.....	2%-20%	4%-7%
Creatinine.....	1.2-1.5	1.2-1.6
Blood urea nitrogen.....	14-30.3	10-28.5
Sedimentation rate.....	0.4-1	0.4-1.7

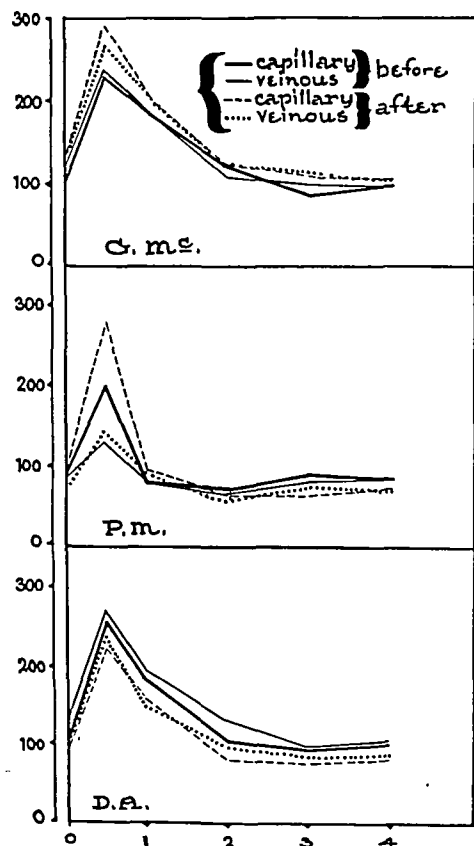


Chart 1.—Dextrose tolerance curves before and after administration of stilbestrol in 3 patients.

with any other estrogenic substance tried. A total of 25 per cent reported an equal result, while 28 per cent reported less success.

As objective signs of improvement we have taken the decrease or disappearance of the gonadotropic substance in the urine of pregnancy and the appearance of estrus as evidenced by the vaginal smear method and the determination of the urinary estrogens. From table 2 we learn that 64 per cent of the patients treated at least for one month with stilbestrol showed no significant amount of gonadotropic substance in the urine as contrasted to only 23 per cent of the untreated control group, while over half of the treated patients showed a large amount of estrogenic substances. The vaginal smear changed in almost all instances within the first week of treatment from a menopausal to an estrogenic type. Changes in the endometrium were not observed

strual period and lasted up to twenty-one days. Curettage revealed a moderate or marked proliferation of the endometrium without evidence of the secretory phase. Vaginal discharge was observed in 7 cases. Mammary symptoms consisting of painful fullness of the breast, and some nodular swellings were present in 5 cases. Increased sexual stimulation was present in 3 cases. In those climacteric women who were still menstruating while under treatment, stilbestrol therapy affected the menstruation. Three menstrual periods were delayed, and one stopped; in 11 cases cramps accompanying the period were increased or appeared, and at the same time the patient complained of headache.

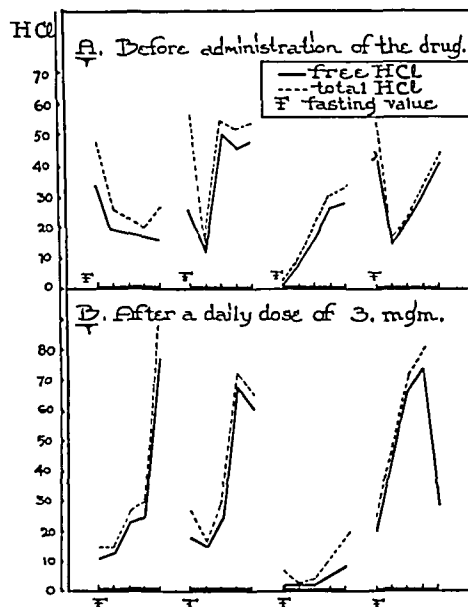


Chart 2.—Gastric analysis after alcohol test meal in 4 patients treated with small doses of stilbestrol.

We may say that stilbestrol has proved to us, in the doses administered orally to patients, a powerful estrogenic substance. It is our opinion that most of the doses recommended so far in the literature are excessive and that smaller doses should be used. We believe also that its continuous administration is unnecessary and that it should best be spaced at regular intervals. By using discretion in its administration an excessive stimulation of the sexual organs can well be avoided.

although this stimulation seemed in no way harmful and in no way different from the effects produced by excessive doses of natural estrogen. We feel, furthermore, that the more intelligent type of patient, who shows better cooperation with the physician, will receive greater advantages from the treatment.

CLINICAL STUDIES OF TOXICITY

Already the earliest investigators of stilbestrol have observed that its oral administration caused a number of untoward symptoms in patients which were sometimes so pronounced that the administration of the drug had to be discontinued. Reports of the incidence of these so-called toxic effects vary and are probably dependent a great deal on the type of patients and the carefulness of clinical observation. In the brief tabulation of the toxic symptoms as cited so far in the literature we observe a remarkable variation of incidence reported by the various authors (table 3). The symptomatology of stilbestrol has been best studied by Shorr, Robinson and Papanicolaou¹⁸ and by Varangot.¹³ Shorr and his associates found lassitude the most prominent symptom. They observed in their series 6 patients with vertigo, 8 with erythema, 1 with toxic psychosis, 1 with paresthesia and 1 patient afflicted with unquenchable thirst. As a rule these symptoms persisted, and a second course of treatment was tolerated as poorly as the first. Toxic reactions were also obtained two to three hours after injection of stilbestrol. Their appearance could not be correlated with any critical level, and Shorr and his associates postulated that all indications pointed to an injury to the central nervous system as their cause. Varangot distinguished between early and late toxic symptoms after administration of stilbestrol.

after meals with nausea, vomiting and vertigo. Loss of appetite and general malaise were present, and the patient urgently insisted on discontinuance of the therapy.

Available laboratory reports have so far failed to show any tangible evidence of toxicity in human beings. The

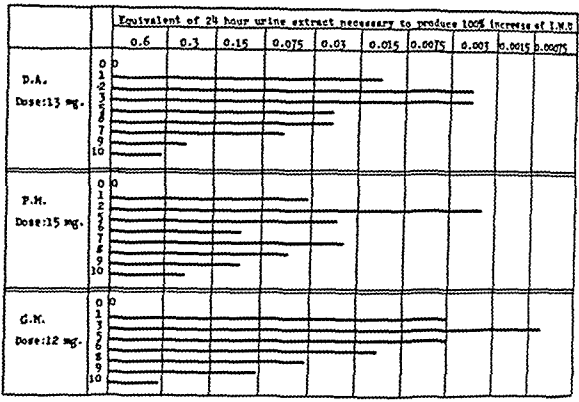


Chart 4.—Urinary excretion of stilbestrol, in 3 patients after injection of 1 mg. to 10 pounds (4.5 Kg.) of body weight. I. M. U., infantile mouse uterus.

tests involved include red blood cell counts; leukocyte counts; hemoglobin determinations; urinalyses; serum protein determinations; icterus index and van den Bergh reactions; bromsulphalein, galactose and hippuric acid tests, and prothrombin determinations (MacBryde and his co-workers, Buxton and Engle²³ and Shorr and his co-workers). No evidence of allergic or urticarial phenomena was obtained.

In section 5 of our clinical summary (table 1) the so-called toxic symptoms encountered during treatment with stilbestrol are analyzed. A total of 52 patients, or approximately 42 per cent, complained of some untoward symptoms during treatment. In the majority of cases nausea and vomiting were the principal and only cause of complaint. Headaches and dizziness rated second in importance. One case of psychotic excitement and 2 cases of severe diarrhea occurred during stilbestrol therapy. One exceedingly sensitive patient had a severe local reaction consisting of vaginal discharge, cystitis, backache, itching of the vulva and marked stimulation of the breast on a total dose of 3 mg. given orally in 0.5 mg. doses for six days. In another patient there developed in the course of treatment a galactocoele of the breast.

In the clinical evaluation of the aforementioned symptoms we may state that although they were decidedly disagreeable they appeared not in any way seriously harmful and disappeared in all instances as soon as treatment with stilbestrol was discontinued. They could be observed either immediately after the first administration of the drug or shortly thereafter and were likely to develop more frequently after oral administration, although parenteral administration occasionally produced them. Reduction in the dose usually decreased the severity of these symptoms sufficiently so that the patient could carry on with the treatment. Only in 9 cases were we forced to discontinue the therapy. Our attempt to avoid the gastrointestinal symptoms by administering the drug in enteric coated tablets has met with failure so far; 5 out of the 6 patients treated in this manner became nauseated.

A series of clinical investigations was undertaken with the purpose of discovering definite evidence of toxicity

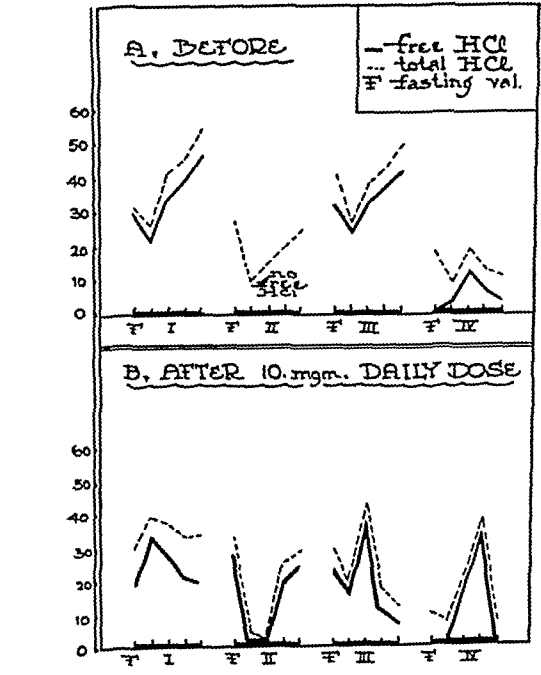


Chart 3.—Gastric analysis after alcohol test meal in 4 patients treated with nauseating doses of stilbestrol.

Usually the patient was taken ill on the second day with feelings of nausea and vomiting. Even if the administration of stilbestrol was immediately stopped, the complaints persisted for one to two days. Continuation of treatment made the complaints more accentuated. The late symptoms, which set in after two months of treatment, consisted of burning gastric pain occurring

23. Buxton, C. L., and Engle, E. T.: Effects of the Therapeutic Use of Diethylstilbestrol, J. A. M. A. 113: 2318 (Dec. 23) 1939.

of the drug in the doses administered to human beings. Our study was conducted on men and women patients who were admitted to the hospital and treated with doses of stilbestrol. Repeated, and in one instance daily, blood counts were done with determinations of all formed elements in the blood. Although occasionally an abnormally low value was obtained, such as 152,000 for thrombocytes or 3,500,000 for red blood cells, in no instance could any evidence of a permanent injury to the blood be obtained (table 4). A specimen of bone marrow which we took for biopsy from a patient with a low red blood cell count showed hyperplasia of the erythropoietic elements and a small increase in the monocytes and eosinophil myelocytes. The blood sugar curves determined on 3 patients who obtained one single large dose of stilbestrol showed no consistent changes in the dextrose tolerance (fig. 1).

Because of the predominance of gastrointestinal symptoms gastric analysis was performed before and after administration of stilbestrol. In one group of patients small doses which did not produce any nausea were given over three days. Although the acid value while the patient was fasting was lower than before administration of the drug, the acidity rose to a higher peak after an alcohol test meal (fig. 2). We then administered to 4 patients doses of 10 mg. daily, which produced severe nausea with vomiting. The analysis of the gastric secretion showed irregular curves, which, however, inclined more to the side of hypoacidity (fig. 3). With reference to our animal experiments in which we definitely observed mucosal atrophy of the stomach after toxic doses, we suggest that small doses of stilbestrol may exert an irritating effect, while large doses have a depressing effect on the gastric secretion. It is the latter factor which probably is responsible for the nausea.

All other laboratory tests which were done on the patients before and after treatment with stilbestrol failed to show any evidence of organic injury (table 5). The liver function, as determined by the icterus index, the prothrombin level of the blood, the Weltmann coagulation band, the serum bilirubin and the bromsulphalein test, was normal in all our patients. The kidney function, as determined by the blood urea nitrogen and the blood creatinine, was not impaired. The urine of the patients showed in no instance albumin or casts. The blood chlorides (Selye²⁴) were not changed.

In order to determine the fate of the injected stilbestrol, the excretion of the substance was determined quantitatively in the urine and feces of 3 patients who received one large dose of the drug (10 to 15 mg.). Figure 4 shows the daily excretion in the urine as measured by the equivalents of twenty-four hour urine extracts which were necessary to produce 100 per cent increase of the infantile mouse uterus.²⁵ The excretion of the drug in the urine begins immediately after its administration, reaches its highest levels on the third to the fifth day and decreases rapidly to a small amount, which then can be found in the urine for some time. We carried on the determinations for sixteen to twenty days, until even the last trace of the substance had disappeared. The feces during this period gave a strong estrogenic reaction, and we must assume that a considerable portion of the ingested stilbestrol is excreted with the feces. An approximate calculation of the

excreted amount would suggest that from 10 to 30 per cent of the ingested stilbestrol was excreted within the first ten days after its administration.

SUMMARY AND CONCLUSIONS

One hundred and twenty-five patients with surgical and natural menopause were treated from two weeks to six months with doses ranging up to 60 mg. of stilbestrol. In 75 per cent of the cases excellent or good results were obtained, with 39 per cent of the patients reporting better response to this therapy than to any other estrogenic substance used previously. In 42 per cent of the patients some untoward symptoms appeared during the therapy. These, however, could be controlled in the majority of cases by reducing the dose, and the treatment had to be discontinued in only 9 cases.

Laboratory investigation of the function of the parenchymatous organs and of the erythropoietic system did not reveal any evidence of organic injury. A gastric analysis showed a slightly decreased response of the mucosa to the alcohol test meal after the administration of nauseating doses of the drug. Ten to 30 per cent of the ingested stilbestrol was excreted in the urine and feces during the first ten days following its administration.

We feel that because of the ease of administration and the great economic advantages stilbestrol has a definite place in the treatment of the menopause provided that small doses are used and that the therapy is not continued over too long a time.

Clinical Notes, Suggestions and New Instruments

DERMATITIS DUE TO A FACE POWDER CONVEYOR

LESTER HOLLANDER, M.D., PITTSBURGH

Mrs. R. H., aged 49, an American housewife, referred to me by Dr. Charles E. Hays of Johnstown, Pa., on May 7, 1940, presented a sharply defined, vesiculo-erythematous eruption which involved the nose, the upper lip and the adjacent portion of the right lower eyelid. The tip of the nose and the central furrow of the upper lip were thickened and cracked, these being the areas of the most marked involvement. The eruption was of approximately four months' duration and it was exceedingly itchy.

It was evidently due to some sensitizing contact substance, but neither the history of the onset and course nor any variability in the intensity of the subjective symptoms gave me any clue except that the substance had something to do with the face and especially with the nose.

Accordingly the patient was instructed to stop the use of her cosmetics, soap, handkerchiefs and cleansing tissues for a period of two weeks. At the expiration of that period she returned; her face was practically clear, indicating that I was on the right track. Patch tests were now done with all the interdicted substances and articles, including face powder, rouge, lipstick, nail lacquer, cleansing and tissue creams, perfume, wave set, soap and cleansing tissue. These were negative at the end of forty-eight hours and also at the end of one week.

Because of the clinical improvement after the discontinuance of her cosmetics and soap she was instructed to return to the use of these singly, one week apart, so as to ascertain the cause as the eruption would reappear.

On August 7 she returned with a marked recurrence of the eruption. I was unable to trace back the irritant because, after being free from the eruption for a few weeks, the patient returned to her regular cosmetic and cleansing routine.

I decided to retest her to her cosmetics. In obtaining the various samples for the patch tests her face powder was pro-

24. Selye, Hans: On the Toxicity of Oestrogens with Special Reference to Diethylstilbestrol, *Canad. M. A. J.* 41: 48, 1939.

25. von Haam, Emmerich: The Direct and Indirect Determinations of Estrogenic and Gonadotropic Hormones, *Am. J. Clin. Path.* 10: 205, 1940.

duced from a rubber sponge powder puff. It was rounded and biscuit-like with a central pocket reached through a lateral slit. The porous quality of the rubber permitted the escape of the face powder when the skin was patted with the puff. She bought this puff shortly before the original onset of this eruption and used the puff to powder her nose only when she was away from her home. The outline of the eruption was confined to the area of its use.

Patch tests of the puff, with and without the face powder, were strongly positive in twenty-four hours, while the patch test of the face powder alone was again negative.

This case is of interest because a dermatitis was produced by a conveyor of a cosmetic, a rubber sponge powder puff, and there is no mention of such an occurrence in the literature. 631 Jenkins Building.

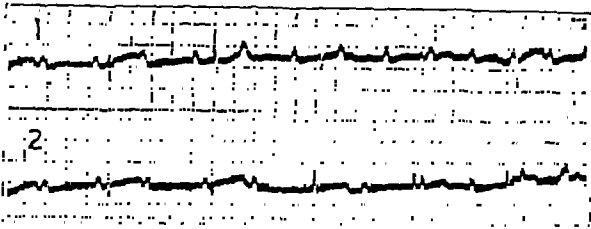
PRENATAL DIAGNOSIS OF COMPLETE CONGENITAL HEART BLOCK

Clyde J. Geiger, M.D., and Laurence E. Hines, M.D.
Chicago

About seventy cases of congenital heart block have been recorded. Yater's¹ review of cases prior to 1929 included only thirty cases of well established block. The criteria used by him and in subsequent reviews were auriculoventricular dissociation proved by a graphic method in a relatively young person, development of bradycardia at a fairly early age, and absence of a history of infection which might cause heart block. In 1934 Hays² collected twelve additional cases. Since then about twenty-six additional cases have been reported. The age at which the diagnosis of heart block has been made varies from birth up to 20 years. Only five cases including our case have been diagnosed before birth. Yater,¹ Witt,³ Heubner⁴ and Ottow⁵ have made a prenatal diagnosis of complete heart

REPORT OF CASE

Mrs. F. H., a white primipara aged 30, a patient of Dr. E. W. Mosley, was admitted to the obstetric service at St. Joseph Hospital Dec. 2, 1939. Her antepartum course had been uneventful. She had had no serious illnesses or operations in the past. She was well nourished and presented the usual manifestations



Leads 1 and 2 of electrocardiogram.

of pregnancy at full term, blood pressure 116 systolic, 86 diastolic, a negative Wassermann reaction, a normal blood count and normal urine. At the time of admission the bag of waters was intact, the head was not engaged, labor pains were mild and irregular and the fetal heart tones were 136 per minute. Two hours after admission the labor pains were still mild and irregular. No engagement of the head had taken place but the fetal heart tones had dropped to 64 per minute. The slow fetal heart rate varying from 58 to 64 per minute persisted until the time of delivery, which occurred nineteen hours after admission. At first the sharp drop in fetal heart rate caused suspicion of impending fetal asphyxia. However, the persistence of regular forceful beats between pains was not characteristic of asphyxia and a diagnosis of heart block was considered and labor was allowed to proceed normally. A healthy female infant weighing 3,180 Gm. delivered spontaneously forty-eight

Review of Previously Reported Cases of Prenatal Diagnosis of Heart Block

Author	Sex	Slowest Fetal Heart Rate	Slowest Rate After Birth	Time of Prenatal Diagnosis	Malformations	Heart Enlargement	Proof of Block	Cyanosis	Duration of Life	Other Observations
Yater 1929	♂	47	47	2 weeks	Numerous anomalies (autopsy)	0	Positive electrocardiogram	4 plus	18 days	Died in cyanotic attack
Witt 1934	♂	44	44	2 months	Concretion of aorta; endocardial defect (autopsy)	4 plus	Positive electrocardiogram	4 plus	75 days	Died in cyanotic attack
Heubner 1938	No record	80	60	Not given	None	0	Positive electrocardiogram	0	Living at 11 months (healthy)	Block disappeared at 11 months
Ottow 1939	♀	32	52	24 hours	None	1 plus (left)	Positive electrocardiogram	0	Living at 5 months (healthy)	Block still present at 5 months
Geiger and Hines 1940	♀	58	60	17 hours	None	0	Positive electrocardiogram	0	Living at 5 months (healthy)	Block still present at 5 months

block. The diagnosis of heart block before birth has also been made by White, Eustis and Kerr,⁶ Maclellan,⁷ Dippel,⁸ Kriszt⁹ and Philipp,¹⁰ but these were reports of partial (not complete) heart block.

1. Yater, W. M.: Congenital Heart Block: Review of Literature; Report of Case with Incomplete Heterotaxy; Electrocardiogram in Dextrocardia, *Am. J. Dis. Child.* 38: 112-136 (July) 1929.
2. Hays, Luvern: Report of Three Cases with Résumé of Literature to Date, *J. P. Dis. Child.* 47: 380-387 (Feb.) 1934.
3. Witt, D. B.: Congenital Complete Heart Block, *Am. J. Dis. Child.* 47: 380-387 (Feb.) 1934.
4. Heubner, Dietrich: Ueber die Bedeutung von Herzblock bei Neugeborenen, *Ztschr. f. Kreislaufforsch.* 30: 600-602 (Aug. 15) 1938.
5. Ottow, Benno: Intrauterine Wahrscheinlichkeitsdiagnose eines Herzblocks bei der Frucht—klinisch am Neugeborenen bestätigt, *Zentralbl. f. Gynäk.* 63: 715-719 (April 1) 1939.
6. White, P. D.; Eustis, R. S., and Kerr, W. J.: Congenital Heart Block, *Am. J. Dis. Child.* 22: 299-306 (Sept.) 1921.
7. Maclellan, E. K.: Double Placenta Praevia (Binovular Twins) and Prenatal Diagnosis of Congenital Heart in Successive Labors, *Brit. M. J.* 1: 14-15 (Jan. 5) 1935.
8. Dippel, A. L.: Two Cases of Congenital Heart Disease in Which Diagnosis Was Made Before Birth, *Am. J. Obst. & Gynec.* 27: 120-123 (Jan.) 1934.
9. Kriszt, Josef: Angeborener sino-aurikulärer Block bei einem Neugeborenen, *Zentralbl. f. Gynäk.* 61: 2515-2518 (Oct. 23) 1937.
10. Philipp, Ernst: Angeborener kindlicher Herzfehler, intrauterin wahrgenommen, *Ztschr. f. Geburtsh. u. Gynäk.* 91: 665-668, 1927.

minutes after the beginning of the second stage of labor. The baby and mother were discharged in apparent good health nine days after the birth. The infant was well nourished and healthy. There was no cyanosis, no enlargement of the heart, no murmurs and no abnormal accentuations. Repeated electrocardiograms, one of which is shown in the illustration, revealed complete heart block with an auricular rate of 120 and a ventricular rate of 60, right axis deviation and flat T waves in all leads. A roentgenogram of the chest revealed a heart and aorta of normal size and contour. The retrocardiac space was clear. The lung fields were well aerated. April 1, 1940, the baby was in good health except for the heart block, which a recent electrocardiogram showed was still present.

COMMENT

Prenatal diagnosis of complete heart block has been reported only five times. The accompanying table includes the important information in the five reported cases. The time of diagnosis prior to birth varied from seventeen hours to two months. In all instances the diagnosis was made by detection of an unusually slow regular fetal heart rate (32 to 80). All

diagnoses were confirmed by electrocardiograms, which showed complete auriculoventricular dissociation. In our case a differentiation between asphyxia and heart block was necessary because the onset of block occurred during the course of labor. Asphyxia as the cause of fetal bradycardia was ruled out in this case because the rate was constant and the strength and regularity were not influenced by uterine contractions.

Necropsies on patients with congenital heart block usually have shown congenital malformations. Two patients of this series died and autopsies revealed congenital anomalies in each. Both fatal cases also showed typical clinical evidence of congenital defects, as evidenced by cyanosis, murmurs and enlargement. However, the other three, all living, showed no clinical evidence of congenital defects, and it is possible that other transient lesions of the bundle of His may cause the block. Hemorrhage or toxic or inflammatory lesions might reasonably produce a temporary defect. This is suggested by the termination of the block in Heubner's case and also by the termination of partial block in other cases. The absence of toxemia in the mother and the development of the block early in labor lend no support to hemorrhage or infection as an etiologic factor in our case.

The presence of cyanosis and of other signs of congenital heart defects in patients with complete congenital heart block points to an early unfavorable prognosis. If the block is not associated with clinical evidence of congenital defects, the health of the child may be unimpaired and the prognosis less serious.

SUMMARY

A case of complete heart block was diagnosed before birth. A sudden slowing of the fetal heart rate which occurred between seventeen and nineteen hours before birth points to the onset of the abnormal mechanism at a specific time. The sudden onset of the heart block demanded a differential diagnosis between heart block and intra-uterine asphyxia. No anatomic abnormalities in the heart have been demonstrated, and the child is alive and healthy at 5 months of age.

4753 Broadway.

COLLES FRACTURE SPLINT

VERNON L. HART, M.D., MINNEAPOLIS

Numerous types of splints have been described for maintaining the reduction of a Colles fracture of the wrist. I have used many of them—nonpadded plaster, wooden, sugar tong plaster, anterior and posterior plaster molds, Schede's splint and commercial form-fit splints—but now regularly use the plaster splint to be described because it is easily applied, comfortable and efficient and it prevents complications. The two most distressing complications not infrequently observed are recur-

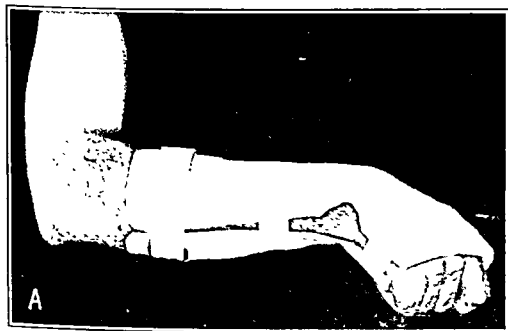


Fig. 1.—Ulnar view of plaster splint showing strip of plaster removed from the ulnar side of the entire splint, plaster removed from the ulnar styloid prominence, and complete flexion of interphalangeal and metacarpophalangeal joints.

rence of radial deviation deformity of the distal fragment of the radius and hand and loss of function of the fingers and thumb because of adhesions and contractures of tendon sheaths and tendons. The plaster splint is applied over stockinet. Not more than two or three 4 inch plaster of paris rolls are used.

No padding is used except for a small piece of felt over the radial or thumb site of the second metacarpal bone. Pressure at this point (fig. 2) is essential in order to maintain reduction of the distal radial fragment and hand in ulnar deviation. The original deformity is radial deviation of the distal radial fragment and hand and this often recurs after perfect reduction if immobilized in splints which do not maintain ulnar deviation.

After the plaster has hardened, a strip of plaster about one-half inch in width is removed from the ulnar side of the splint (fig. 1). This permits the splint to expand and accommodate the swelling which results from hemorrhage. Excessive swelling with edema will not occur if the fractured extremity is continuously elevated during the first several days after the injury.

A niche of plaster also is removed over the prominence of the ulnar styloid process to prevent pressure necrosis and pain.

The plaster is cut away so that complete flexion will be possible at the interphalangeal and metacarpophalangeal joints of the fingers (fig. 1). The second metacarpophalangeal joint will be slightly limited in flexion because of the extension of plaster along the thumb side of the second metacarpal.

Plaster is next cut away to permit complete range of all motions of the thumb. The window at the thumb is extended proximally to remove plaster pressure and prevent pressure necrosis and pain at the base of the thumb or first carpometacarpal area (figs. 2 and 3). The plaster extends over the extensor surface of the metacarpals to the knuckles to maintain the position of the reduction in palmar flexion (fig. 2).

If x-ray studies demonstrate good reduction, the splint should be worn continually from four to six weeks. The patient is instructed to flex and extend all interphalangeal and meta-



Fig. 2.—Extensor view of splint which demonstrates the plaster pressure over the radial side of the second metacarpal bone to maintain reduction in ulnar deviation, the thumb window, plaster removed from ulnar styloid, and plaster extension to knuckles.

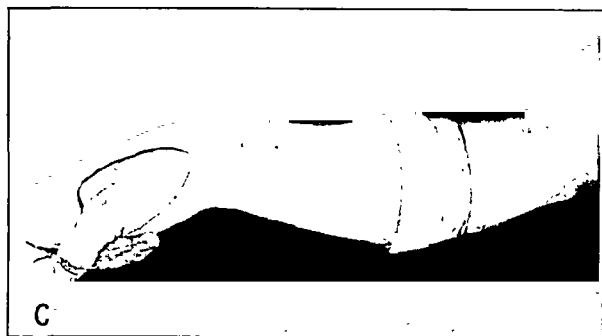


Fig. 3.—Radial view of splint which shows the thumb window and extension of plaster over the radial side of the second metacarpal bone.

carpophalangeal joints of the thumb and fingers completely and actively. Also the patient is instructed to rotate the thumb by touching the tip of the thumb to the end of each individual finger and to abduct and adduct the thumb and fingers. Supination and pronation of the forearm should be encouraged. The elbow and shoulder joints should be moved actively through the normal range of all motions. Besides these active subjective exercises the patient should be encouraged to perform active objective exercises by using the extremity for such activities as eating, dressing and combing the hair. Many patients may even return to their normal occupation after several days.

Massage, light treatments and passive exercises should have no place in the therapeutic program of a fresh Colles fracture.

GLANDULAR PHYSIOLOGY AND
THERAPYLACTOGENIC AND MAMMOGENIC
HORMONES

OSCAR RIDDLE, Ph.D., LL.D.

COLD SPRING HARBOR, N. Y.

This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in these articles are those of the authors and not the official views of the Council.—Ed.

Investigations of the past twelve years provide much new information concerning the regulation of growth and of secretion in the mammary glands. Both growth and secretion are controlled mainly by hormones, but quite different hormones are involved in these two wholly distinct sets of processes. The anterior lobe of the pituitary exercises a direct control (through its lactogenic hormone, prolactin) over milk secretion; in addition it exercises an indirect control (through estrogen, progesterone and possibly other sterols) and perhaps also a direct control (through a mammogenic pituitary hormone) over the development and growth of the mammary glands.

THE LACTOGENIC HORMONE

The Lactogenic Response.—Stricker and Grüter demonstrated in 1928-1929 that a factor or combination of factors directly essential to lactation is produced by the anterior lobe of the pituitary. Their results were confirmed first by Corner in 1930 and thereafter extended to various species by Nelson and Pfiffner, Turner and Gardner, Asdell and others. Indeed both mammary proliferation and lactation were observed to follow the administration of crude pituitary extracts in females with intact ovaries by Parkes in 1929 (rabbits), by Putnam, Benedict and Teel (bitches) and by Evans and Simpson (rats), but this effect either was or could then be attributed to pituitary influence on hormone production in the ovary. A related response, the enlargement of the crop sacs of pigeons with formation of "crop milk," was reported in 1931 by Riddle and Braucher. All these results were obtained with simple glandular extracts—mixtures of various pituitary products—and provided no indication of the identity of the hormone or hormones that excited this response.

Isolation and Identification of the Hormone.—The individuality of the hormone that excites lactation was established in 1932-1933 through its isolation and study by Riddle, Bates and Dykshorn,¹ who definitely associated it with lactogenic and crop-stimulating functions and called it prolactin. Confirmation of its individuality and lactogenic function was soon supplied by Catchpole and Lyons² and Lyons and other associates,³ who called the hormone mammatropin, and by Gardner

and Turner,⁴ who also fully described the mammary changes accompanying its lactogenic action in the rabbit. Gardner and Turner called this hormone galactin.

Occurrence.—The hormone is probably present in the hypophyses of all vertebrates but is more plentiful in some species and at certain stages of the life cycle than others. Beef and sheep glands usually yield 30 to 40 international units per gram of fresh tissue, while pork glands contain much less.⁵ Pituitaries of fetal calves were once reported⁶ to contain much more prolactin (78 + units) than the glands of adult or pregnant cows (38-44 units), but a later report⁷ stated these values in essentially the reverse order. In the study represented in the latter report a higher concentration of hormone was found in glands from dairy cattle than in those from beef cattle, and in both studies a somewhat higher concentration was found in glands from pregnant (or lactating) cows than in those of heifers. There is evidence that prolactin is formed in the eosinophilic cells⁸ and that administration of estrogen increases the amount of it (stored?) in the rat gland.⁹ Small amounts have been found repeatedly in postpartum human urine (also in urine of normal men and in that of infants during the first week) since this was first reported by Lyons and Page,¹⁰ who stated that the amount excreted daily is equal to that found in one beef pituitary. It is alleged that two peaks of excretion occur within the normal cycle of the female sex: during menstruation and during ovulation.¹¹ Positive tests were reported for human serum¹² and for young (not for mature) placentas¹³ and notable quantities from cystic human breasts.¹⁴ Hoffmann¹⁵ found less than the expected amounts of prolactin in the urine of seven of eight parturient women whose secretion of milk was subnormal. Rabald and Voss¹⁶ reported recovery of a prolactin-like substance from the livers of healthy cattle and hogs but not from horse liver.

Preparation and Assay.—Currently used methods of preparing¹⁷ prolactin from pituitary tissue involve its initial extraction in acid or alkaline medium (aqueous or 60 per cent alcohol [ethyl alcohol], or acid acetone), its isoelectric precipitation in an aqueous medium and repeated washing of this precipitate. Comparisons of the various methods are available.¹⁸ Current methods of assaying prolactin were surveyed by McShan and Turner,¹⁹ Bergman and Turner,²⁰ and Bates;²¹ crop sacs of

4. Gardner, W. U., and Turner, C. W.: The Function, Assay and Preparation of Galactin, a Lactation Stimulating Hormone of the Anterior Pituitary and an Investigation of the Factors Responsible for the Control of Normal Lactation, research bulletin 196, University of Missouri, College of Agriculture, Agricultural Experiment Station, 1933, pp. 1-60.

5. Bates, R. W., and Riddle, Oscar: The Preparation of Prolactin, J. Pharmacol. & Exper. Therap. 55: 365 (Nov.) 1935.

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14. Geschickter, C. F., and Lewis, Dean: Lactogenic Substance in the Human Breast, Arch. Surg. 32: 598 (April) 1936.

15. Hoffmann, Friedrich: Ueber die hypophysäre Hypogalaktie, Zentralbl. f. Gynäk. 61: 35 (Jan. 2) 1937.

16. Rabald, E., and Voss, H. E.: Ueber Vorkommen und Eigenschaften des Laktationshormons, Ztschr. f. physiol. Chem. 261: 71, 1939.

17. Bates and Riddle.⁵ McShan and Turner.¹⁹ Lyons.²¹

18. Riddle, Oscar, and Bates, R. W.: The Preparation, Assay and Actions of Lactogenic Hormone, in Allen, Edgar, Danforth, C. H., and Doisy, E. A.: Sex and Internal Secretions, ed. 2, Baltimore, Williams & Wilkins Company, 1939, chap. 20, p. 1088. Bergman and Turner.²⁰

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4. V. R.; Chaikoff, I. L., and Reichert, J. L.: Lactogenic Hormone on Normal, Dogs, *ibid.*, p. 303. Lyons, W. R.,

5. Ovary and Catchpole, H. R.: Assay of the Hypophysial Lactogenic Hormone, *ibid.*, p. 305.

pigeons (macro and micro tests available) or of lactation in pseudopregnant rabbits. The micro test in pigeons is said to be sensitive to 0.01 microgram of lactogenic hormone.²²

For assay of this hormone in urine (or serum) Lyons²² now injects unconcentrated urine intradermally (micro test) over the crop sacs of pigeons 1 month old. Four daily injections (0.05 to 0.5 cc.) are made at five sites on each crop gland (feathers removed), with necropsy twenty-four hours after the last injection. After stripping away the muscle and the inflammatory exudate which always results from the toxic substances in the urine and which masks minimal reactions, the crop wall is inspected against good light for stimulation at the sites of injection. By using varying quantities on a few birds, a standard or minimal effective dose of the urine (preserved with hexylresorcinol) is determined.

Four quite different macro units ("pigeon units") now confuse the literature, but a practical solution is at hand. A standard preparation of the lactogenic (crop gland-stimulating) substance—to be distributed on behalf of the League of Nations Health Organization—is available from the National Institute for Medical Research, Hampstead, London, England. Samples made in different laboratories were combined to form this standard preparation, and it was decided that "agreement shall be reached among the members of the Conference as to the activity of the standard preparation in 'Riddle-Bates units' per milligramme, and that the international unit shall be thus defined in terms of the standard preparation."²³

Properties.—Prolactin is insoluble in all fat solvents. It is soluble in water except in the isoelectric region pH 5-6 and in strongly acid solution, < 0.5 . When made acid to the isoelectric point, the extract containing prolactin is precipitated by the usual protein precipitants—e. g., by tannic, phosphotungstic, flavianic and trichloroacetic acids and by trinitrophenol. It may be salted out with sodium (or ammonium) sulfate or sodium chloride, the amount required depending on the pH . It is also precipitated by basic salts of heavy metals at or near pH 7.²⁴ It is rapidly inactivated by trypsin²⁵ and pepsin.²⁶ Salt-free solutions at pH 8 withstand boiling for one hour with little loss; under other conditions the prolactin may be rapidly destroyed.²⁷ A crystalline protein with fairly high lactogenic activity was extensively studied by White, Catchpole and Long²⁸ and found to have the following elemental composition in percentage: carbon 51.11, hydrogen 6.76, nitrogen 14.38, sulfur 1.77, phosphorus 0. In their better preparations of prolactin Bates and Riddle²⁹ found roughly 2 per cent each of tyrosine, cystine and tryptophan. Tests indicated that free amino groups in prolactin are essential to its activity.³⁰ More advance has been made in the chemical study of prolactin than in that of any other anterior pituitary hormone.

Applications and Actions.—For increasing the milk yield of domestic animals after lactation has been established or during declining lactation, prolactin has sometimes³¹ but not always proved efficacious; likewise, from whole pituitary extracts both success and failure

are recorded;³² still other glandular products (notably thyroxine)³³ have sometimes proved of equal or of greater effectiveness for these unusual requirements. Again, the adrenal cortex—perhaps incident to its regulation of fluid and salts or to the production of sterols supporting mammary growth—seems to contribute something essential to the maintenance of milk flow or even to the initiation of this function in some species,³⁴ though apparently not in the dog.³⁵ Similarly, hypophysectomy, thyroidectomy or hysterectomy may markedly affect lactation. Finally, estrogen, though certainly helpful in the preparation of mammary tissue, becomes for one true action of prolactin an agent decidedly adverse to milk yield after lactation has been established.³⁶

Since it is thus obvious that so much of the organism—assimilative, endocrine and neural—becomes involved in the initiation, augmentation and maintenance of lactation, the term "lactogenic hormone" is equivocal and its use often a serious error; others (not ourselves) have rather generally ventured to employ this term as an alternative designation for that hormone which was found to initiate milk secretion in prepared mammary tissue and which after its isolation and establishment as an entity was called prolactin. Lactogenesis involves several hormones and many other factors; prolactin is a specific substance. Only full recognition of this distinction, along with awareness of other actions of prolactin, is likely to lead to satisfactory clinical use of this substance.

Clinical use of prolactin hitherto has been restricted largely to postpartum women with deficient lactation. In the earliest tests³⁷ twenty-nine women whose lactation had failed to develop adequately by the sixth to the ninth day were then given one or two intramuscular injections of prolactin, totaling 75 to 400 units. This dosage (highest, 200 units per injection) was well tolerated. In twenty-five of these women the daily milk yield increased by from 50 to 400 Gm. within three to nine days; there were four or five definite failures, in all of which the total dose used was only 100 to 150 units. In eight other women, whose milk secretion was or presumably would become normal, dosage for a single day with 100 to 400 units at one to fifteen days post partum probably induced no change. Werner³⁸ noted that eight castrates whose breasts were variously prepared (or unprepared) by previous estrogenic treatment did not lactate after intramuscular injection of 200 units of prolactin daily

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27. Riddle, Bates and Dykshorn.^{1c} McShan and French.

28. White, Abraham; Catchpole, H. R., and Long, C. N. H.: A Crystalline Protein with High Lactogenic Activity, Science 86: 82 (July 23) 1937.

29. Riddle and Bates,¹³ p. 1093.

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Folley, S. J., and Young, F. G.: The Effect of Anterior Pituitary Extracts on Established Lactation in the Cow, Proc. Roy. Soc., London, s. B 126: 45 (Sept. 23) 1938. Azimoff.³²

32. Azimoff, G. I.: Probleme der Laktationsphysiologie, in Proceedings of the Fifteenth International Physiological Congress, Leningrad-Moscow, Aug. 9-16, 1935, Moscow, State Biological and Medical Press, 1938, pp. 132-133.

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35. Kendall, E. C.; Mason, H. L.; Myers, C. S., and Allers, W. D.: Physiological and Chemical Investigation of the Suprarenal Cortex, J. Biol. Chem. 114: lvii (May) 1936; personal communication to the author.

36. Parkes, A. S., and Bellerby, C. W.: The Effects of Injection of Estrin During Lactation, J. Physiol. 62: 301 (Jan.) 1927. De Jongh, S. E.: Laktationshemmung durch Menformon, Acta brev. Neerland. 3: 52, 1933. Nelson, W. O.: The Reciprocal Hypophyseal Ovarian Relationship as a Factor in the Control of Lactation, Endocrinology 18: 33 (Jan.-Feb.) 1934. Kurzrok, Raphael, and O'Connell, C. P.: The Inhibition of Lactation During the Puerperium by Testosterone Propionate, Endocrinology 22: 476 (Oct.) 1935.

37. Kurzrok, Raphael; Bates, R. W.; Riddle, Oscar, and Miller, E. G., Jr.: The Clinical Use of Prolactin, Endocrinology 18: 18 (Jan.-Feb.) 1934.

38. Werner, A. A.: Experiment to Produce Lactation in Castrate Women, Endocrinology 19: 144 (March-April) 1935.

for one to fourteen days; severe local and systemic reactions were produced in three of these women (two others reported on later). Evans³⁹ briefly reported seven successful tests with total doses of from 1,000 to 2,250 units. Hoffmann⁴⁰ noted that a total dose of 200 to 250 units given in two days may or may not increase the milk yield.

Two recent critical studies on the effects of twice-daily injections during two to four days, beginning on the sixth or seventh day post partum, led to somewhat different conclusions, though there were several obvious failures in both series of tests. Ross,⁴¹ using intramuscular injections during two days, gave a total dose of 400 units to nine patients and 1,000 units to twelve others. Only the larger dose appeared to result in an appreciable increase in milk secretion, and only this dose produced any adverse local reactions; the latter involved redness and indurations varying in diameter from 2 to 15 cm., and a rise in temperature to 100 to 102 F. for two to six days. Considered of special significance was the observation that a higher proportion of the mothers given the larger dose were able to nurse their infants after discharge from the hospital. Stewart and Pratt,⁴² giving a subcutaneous injection of 1,000 units daily from the sixth to the ninth postpartum day inclusive, got no significant increase in milk secretion from a group of fourteen patients whose secretion was less than 250 cc. on the fifth day. A similar group of ten mothers served as controls, and after leaving the hospital their nursing record was not significantly different from that of the group given prolactin. Stewart and Pratt conclude that the action of prolactin in animals is not analogous to that in women.

The most recent study is also the most complete and informative. Kenny and King⁴³ treated forty-three women with prolactin for deficient lactation, beginning at different stages up to the third month post partum; forty-three other women, to whom other "galactogogues" were given or on whom routine methods of encouraging lactation were practiced, served as controls. In 74 per cent of the treated women and in only 21 per cent of the controls lactation became sufficient for the whole need of the baby until weaning at the sixth to the seventh month. The complete failures included 19 per cent of the treated women and 63 per cent of the controls. The total dose of prolactin was 900 units, which was given intramuscularly at the rate of two injections a day for five days, as follows: on the first and second days 300 units a day, on the third and fourth days 120 units a day and on the fifth day 60 units. No local or systemic ill effects were observed. The milk produced was of normal composition and quality. They recommended that treatment begin early in order that efficient nursing might be established before discharge from the hospital.

Other actions of prolactin have been reported from animal experimentation, though appropriate clinical applications have not yet been published. In adult birds prolactin has powerful antigonad action, made evident by extremely rapid and nearly complete atrophy of the testes⁴⁴ and by speedy inactivation and regres-

sion of the ovary.⁴⁵ In adult male rats 10 to 20 units of prolactin daily for eight to fifteen days does not decrease the weight of the testes.⁴⁶ In female mice⁴⁷ and rats⁴⁸ dosage with prolactin stops estrous cycles. Small amounts of luteinizing substance also stop the cycles of mice, and since luteinizing substance is a contaminant of many prolactin preparations it has been suggested⁴⁹ that this action on the cycles of rodents is exercised by the luteinizing substance. Though it is clear that prolactin is, and luteinizing substance is not, effectively antigonad in birds, this action of prolactin is still uncertain in mammals.

Prolactin seems to be specifically involved in the onset or production of broodiness in the fowl,⁵⁰ the maternal or parental instinct in rats⁵¹ and nesting behavior in fish.⁵² Other anterior pituitary extracts, the urinary luteinizing substance, estrone (theelin), progesterone and extract of adrenal cortex all seem ineffective or inhibitory in the fowl, though phenol is active in fish, and pituitary luteinizing extract, intermedin, progesterone, desoxycorticosterone acetate and phenol are all fairly effective in rats.

Prolactin has marked calorogenic action in pigeons—normal, hypophysectomized or thyroidectomized—and its synergistic action with thyrotropin on heat production has been reported in normal doves.⁵³ The relation of prolactin to carbohydrate and fat metabolism is an important but still unsettled problem.⁵⁴ Splanchomegaly exhibited in the liver, pancreas and intestine of the pigeon is associated with the action of prolactin.⁵⁵ Body weight and appetite are especially increased by prolactin in pigeons, and favorable effects of this substance on the growth of the dwarf mouse—with a synergistic effect on growth when prolactin is administered together with thyrotropin—have been reported.⁵⁶

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Large doses of ox pituitary prolactin (probably not entirely free from serum protein) injected daily into adult rabbits or young female monkeys for eighteen or more weeks resulted in the production of antisera capable of inhibiting the growth response in the crop sac of the pigeon and probably of reducing milk secretion in lactating mice.⁵⁷ Preparations of prolactin from ox and sheep glands, apparently free from serum protein, were found to be antigenically indistinguishable, and the serum of rabbits given injections of prolactin from either source usually partly inhibited prolactin action on crop sacs.⁵⁸

MAMMOGENIC HORMONES

The Mammo-genic Response.—Numerous old and new studies clearly prove that hormones of the ovary play a part in the growth of the mammary gland—in most species an estrogen induces (directly or indirectly) duct growth, and an estrogen plus progesterone induces lobule-alveolar development. Androgens, too, were later proved capable of replacing estrogens in the induction of growth in the mammary parenchyma. Still more recently desoxycorticosterone acetate and some phenanthrene and stilbene compounds not now known to occur in the body are reported to cause duct development in normal and castrate males of the species studied.

In hypophysectomized animals, however, the use of estrogens or androgens to develop mammary tissue has usually, though apparently not always, resulted in failure. Such failures together with the recovery of potent lipid extracts from the anterior lobes of pituitary glands which have been recently subjected to ovarian hormones—and other related facts—lead some investigators to believe that the pituitary gland secretes, in addition to its various hormones of protein nature, other (alcohol-ether soluble) hormone(s) with specific ability to induce mammary growth. In this review one needs to consider only literature bearing on (1) the question of whether estrogens, androgens and available phenanthrenes act directly or indirectly on mammary tissue and (2) the intimately related question of the elaboration of specific mammo-genic hormone(s) by the pituitary.

Direct or Indirect Action of Sterols.—Duct development was reported in 4 of 5 hypophysectomized male rats treated for fourteen days with 50 mouse units of estrone twice daily⁵⁹ and in mammary glands transplanted into similar rats.⁶⁰ Rapid mammary involution was observed in rats after hypophysectomy on the sixth day of lactation despite the injection of 100 micrograms of estrone daily; the conclusion was drawn that the pituitary is necessary for the action of estrone on the mammary gland.⁶¹ Mammary involution would be expected to follow the withdrawal of prolactin and the generally adverse effects of hypophysectomy, and it was later reported⁶² that the involution of the lobule-alveolar system of such rats is not rapid but requires at least as long as does its development. Houssay⁶³ observed

test and mammary enlargement in a male hypophysectomized dog given 10,000 international units of estrone daily for fifty-four days.

Estrone plus progestin was observed to cause further mammary development in hypophysectomized castrate rats than did estrone alone,⁶⁴ and the same was observed in guinea pigs similarly operated on.⁶⁵ In 4 hypophysectomized, ovariectomized rabbits given daily for fifteen days injections of 25 rat units of estradiol benzoate and 4 rabbit units of progestin, mammary development approximately equal to that in rabbits incompletely operated on or not operated on was reported.⁶⁶ Corner⁶⁷ had shown much earlier that in castrate rabbits with intact hypophyses progestin alone is without effect, and others⁶⁸ had observed that estrone plus progestin did cause development of the mammarys of such rabbits.

Later studies (since 1935) with estrogens on pituitaryless animals have more often given negative results on mammary growth, but the significance of these failures has been interpreted variously. Mammary growth in such rats was not stimulated by 25 to 500 international units of estradiol benzoate daily for fifteen to forty-five days,⁶⁹ by 20 to 100 units of estrone for twenty to twenty-five days⁷⁰ and only slightly after estrone,⁷¹ even when the general condition of the rat was sustained with pituitary extract.⁷² Selye and Collip⁷² therefore reaffirmed the view that this action of estrone must be through the pituitary. Astwood and his associates⁷³ emphasized the great importance of reduced nutrition incident to hypophysectomy. They observed mammary regression in normal rats on restricted diet during fourteen days, although 5 micrograms of estrone was injected daily. Likewise, in hypophysectomized rats the duct system regressed under estrone dosage, and the authors concluded that such failures provide insufficient evidence that mammary growth is mediated by the pituitary. Other failures of estrogens to support or increase mammary growth in pituitaryless animals were observed in guinea pigs, mice, rabbits, cats and ground squirrels.⁷⁴ Herold and Effkemann⁷⁵ reported no effect of estrogen in normal male and castrate female rats after severing the nerve connection between the pituitary and the midbrain and suggested that estrone acts by way of the diencephalon

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from which impulses reach the pituitary and cause it to secrete a mammary growth factor.

When the pituitary was removed during pregnancy, the effects on mammary growth were unexpected and important. In rats operated on during the second week mammary growth was unaffected, and the usual accumulation of metabolic products in the lobular cells occurred.⁷⁶ In guinea pigs operated on at the fortieth day, with mammarys examined nine to twelve days later, a condition resembling that of normal glands at parturition was found.⁷⁷ In mice it was observed that even after digital abortion of fetuses and hypophysectomy on the twelfth day normal mammary changes occurred if the placentas had been retained;⁷⁸ the presence of the ovaries had earlier been found unessential for mammary growth at this period.⁷⁹ These results recall earlier evidence for an influence of the placenta on both mammary growth and secretion in animals with intact pituitaries.⁸⁰ That this influence may result from the secretion of an estrogen by the placenta, or otherwise, is obvious.

Testosterone and other androgens have been observed to cause mammary development in normal or ovariectomized rats.⁸¹ In hypophysectomized rats little or nothing more than nipple growth is obtained.⁸² In young male mice, not operated on, and in castrated male mice weighing from 15 to 25 Gm., the development of the mammary glands was accomplished with a wide variety of estrogens and androgens and with desoxycorticosterone acetate.⁸³ This result with the last named substance has special importance because (1) it adds the adrenal cortex to the few possible sources of mammogenic stimulation, (2) these cortical products are heat labile (in contrast with many estrogens) and more soluble in fat solvents, (3) such products are probably released from the cortex in increased amounts by estrone dosage in normal rats and pigeons but not or to a less extent after hypophysectomy,⁸⁴ (4) desoxycorticosterone (the only adrenal derivative hitherto tested) was observed in the study cited to have greater mammogenic potency per milligram than either of the five androgenic substances tested and (5) mice of just this type are used for assay of the mammogenic activity of the pituitary tissues and extracts to be described in the following section.

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84. Miller, R. A., and Riddle, Oscar: Stimulation of Adrenal Cortex of Pigeons by Anterior Pituitary Hormones and by Their Secondary Products, *Proc. Soc. Exper. Biol. & Med.* 41: 518 (June) 1939. Selye, Collip and Thomson.⁸⁵

Mammogenic Potency of Pituitary Tissues and Extracts.—Implantation of pituitary tissue was followed by no appreciable mammary development in many tests made on rats.⁸⁶ In other tests, positive results in both ducts and lobules were secured on hypophysectomized male castrate and noncastrate guinea pigs following implantation of tissue from rats previously treated with estrogen.⁸⁶ In pituitaryless male and female guinea pigs a few tests with an extract of adrenal cortex (eschatin) alone or in combination with an estrogen (not named) indicated no mammary growth. Some further tests were reported, together with citations from the literature, indicating the ineffectiveness of thyroxine and of the recognized pituitary substances.⁷⁰ In a later study immature ovariectomized rats and spayed rabbits showed complete mammary development following implantation during twenty-five to thirty days of fresh (or acetone-dried) anterior pituitary tissue from pregnant cows.⁸⁷ In view of these results a new pituitary principle promoting growth in the mammary gland was postulated by Gomez and Turner and called "mammogenic hormone," or mammogen.

Nelson⁸⁸ reported that the mammary development of hypophysectomized immature female rats in which pituitaries from estrogen-treated rats of either sex had been implanted did not exceed or even equal that which followed implantation of normal rat pituitaries. He also announced his failure to confirm the claim of the existence of a specific "mammogenic hormone." Repeating this study, Reece and Leonard⁸⁹ also found no difference in the potency of pituitaries from untreated and estrogen-treated donors, but they noted that implanted glands of both types gave evidence of some growth when the test animals were compared with their untreated hypophysectomized control.

Albino mice were found to respond to pituitary implants and were considered most suitable for assay of mammogen.⁹⁰ The technic of this assay of the factor promoting duct growth involves the daily subcutaneous injection of macerated fresh anterior lobe tissue from pregnant cows or of mammogen-containing extracts for six days with autopsy on the seventh. The mouse unit is defined as the amount of tissue or extract required (per mouse) to produce definite signs of duct development in one or more glands of 50 ± 10 per cent of ten or more male albino mice weighing 15 to 25 Gm.⁹¹ With this technic the mammogen content of the pituitaries from pregnant cows was found greatest at one hundred and fifty days; that of the dairy cow was greater than that of the pregnant beef cow; that of beef heifers with corpora lutea was 40 to 60 per cent greater than that of pregnant beef cows at the one hundred and fifty day peak; steer, bull and fetal

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86. Gomez, E. T.; Turner, C. W., and Reece, R. P.: Growth of Mammary Gland of Hypophysectomized Guinea Pigs, *Proc. Soc. Exper. Biol. & Med.* 36: 286 (April) 1937. Gomez and Turner.⁷⁰

87. Gomez, E. T., and Turner, C. W.: Further Evidence for a Mammogenic Hormone in the Anterior Pituitary, *Proc. Soc. Exper. Biol. & Med.* 37: 607 (Jan.) 1938.

88. Nelson, W. O.: Effect of Pituitary Implants on the Mammary Glands of Hypophysectomized Rats, *Anat. Rec. (suppl.)* 72: 117 (Dec. 25) 1938.

89. Reece, R. P., and Leonard, S. L.: Further Evidence for a Mammogenic Factor in the Rat Hypophysis, *Proc. Soc. Exper. Biol. & Med.* 42: 200 (Oct.) 1939.

90. Lewis, A. A.; Turner, C. W., and Gomez, E. T.: The Biological Assay of the Mammogenic Duct Growth Factor of the Anterior Pituitary, *Endocrinol.* 24: 157 (Feb.) 1939.

91. Lewis, Turner and Gomez.⁹⁰ Lewis and Turner.⁹²

pituitaries showed appreciable amounts of mammogen.⁹² The authors suggested that estrogens lead to the production of a pituitary factor promoting duct growth, progesterone to a factor promoting lobule proliferation.

Lewis and Turner⁹³ observed that acetone and ether drying of prehypophyseal tissue resulted in a loss of 60 per cent of its mammogen content. Extraction of the tissue with several volumes of hot ether-alcohol (1:3) resulted in a preparation (oily residue) containing 1 unit per 3 to 4 mg. and including practically 100 per cent of the potency of the fresh tissue. In their most recent publication⁹² they have stated that their most potent preparation, tested in fourteen mice, gave positive results in 79 per cent at a dosage of 0.25 mg. per mouse. The estrogen content of some preparations was measured and considered far too low to have caused the mammary growth observed. The fact that fresh pituitary tissue containing mammogen caused both duct development and lobule hyperplasia, though the lipid extracts cause only duct development, was regarded as evidence that the lipid solvent separates a duct growth factor from a lobule growth factor.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

LIVER AND STOMACH PREPARATIONS (See New and Nonofficial Remedies, 1940, p. 320).

SOLUTIONS FOR PARENTERAL ADMINISTRATION

TEN CC. SOLUTION LIVER EXTRACT PARENTERAL-LEDERLE.—A sterile aqueous solution containing the nitrogenous nonprotein fraction G of Cohn et al. obtained from fresh mammalian liver, preserved with 0.5 per cent of phenol. The daily parenteral administration of 0.3 cc. has been found to produce the standard reticulocyte response defined as 1 U. S. P. unit (injectable) when assayed in cases of pernicious anemia as required by the Council.

Actions and Uses.—Solution liver extract parenteral-Lederle is proposed for intramuscular injection in the treatment of pernicious anemia. (See general article Liver and Stomach Preparations, New and Nonofficial Remedies, 1940, p. 320.)

Dosage.—To insure optimum dosage for cases of pernicious anemia in remission it is advisable to make an injection of 5 cc. each day for three or four successive days. In a series of cases in which remissions have been thus initiated by the use of solution liver extract parenteral-Lederle there is evidence that injections of 5 cc. every two weeks (or 1 cc. twice weekly if low unit, more frequent dosage is preferred) provide sufficient active material to complete the remission and maintain a satisfactory blood picture. In complicated cases and those with extensive neurologic involvement, the optimum dosage may be much larger and must be determined for each patient.

Manufactured by the Lederle Laboratories, Inc., Pearl River, N. Y.

Vials Solution Liver Extract Parenteral-Lederle, 10 cc.
Concentrated solution liver extract parenteral-Lederle is prepared as follows: A mixture of finely ground liver and water is acidified to the isoelectric point, pH 5.0-5.4. After partial coagulation of the liver proteins is effected by heating to 75-85°C. the pulp is separated by filtration, centrifugation or pressing and the aqueous filtrate is concentrated in vacuo to the consistency of a thin syrup. By careful fractional precipitation with large volumes of alcohol at low temperatures (4°C.) much inactive material (proteins) is precipitated and subsequently discarded. The alcoholic filtrate is concentrated in vacuo and sufficient alcohol added to precipitate the active material (fraction G)

of Cohn et al. (Proceedings of the American Society of Biological Chemistry, *J. Biol. Chem.* 74:1xix [July] 1927). The washed precipitate generally known as "Cohn's fraction G," commonly obtained as a hygroscopic, brownish powder, in addition to the active antianemic factor, contains much inert matter. In order to obtain a concentrate of the active factor as free as possible from inert substances, the solution containing the fraction G of Cohn is treated with a special activated carbon.

After filtering off the carbon the solution containing the active principle is concentrated in vacuo to a point where approximately 2.7 cc. represents the active material obtained from 100 Gm. of liver. Subsequently sufficient phenol is added to make 0.5 per cent in the finished product; volume is adjusted and the solution is sterilized by Berkefeld filtration.

SOLUTIONS FOR PARENTERAL ADMINISTRATION

(See New and Nonofficial Remedies, 1940, p. 327)

PARENTERAL SOLUTION OF LIVER, 5 U. S. P. UNITS PER CC.-NATIONAL DRUG CO.—A sterile aqueous, clear, dark brown solution containing all of the fraction G of the liver extract (Cohn), preserved with 0.5 per cent of phenol. The daily parenteral administration of 0.2 cc. has been found to produce the standard reticulocyte response defined as 1 U. S. P. unit (injectable) when assayed in cases of pernicious anemia as required by the Council.

Actions and Uses.—Parenteral solution of liver-National Drug Company is proposed for intramuscular injection in the treatment of pernicious anemia. See the general article Liver and Stomach Preparations (New and Nonofficial Remedies, 1940, p. 320).

Dosage.—Daily intramuscular injections of 1 cc. for three to four days may be sufficient for the average case. For more severe cases the doses may be raised to from 2 cc. to 4 cc. It is desirable to give at least 20 units (4 cc.) on the first and second days, but it may be advisable in the case of patients who are to receive the larger doses to divide the dose and give one half of the amount into each gluteal muscle. After seven days' interval, 10 units (2.0 cc.) may be administered at weekly intervals. The dosage of course will vary with the individual patient, depending on the degree of complications.

Distributed by the National Drug Company, Philadelphia.

Amput-Vial Parenteral Solution of Liver-National Drug Company, 10 cc. (5 U. S. P. Injectable Units per cc.).

Parenteral solution of liver-National Drug Company in bulk is passed through a Berkefeld filter into a large sterile container and then it is tested for sterility. If the solution is found to be sterile, it is injected intracutaneously in rabbits and subcutaneously in guinea pigs. Rabbits are tested for necrosis; guinea pigs are checked for edema and general reactions. When these tests show that the material is free from reactions, the solution is filled aseptically into sterile 10 cc. ampul vials. After filling, the material is tested for sterility. Ten containers are selected from the entire lot and each is tested for sterility. If any of these ten tested containers shows growth, ten more bottles are tested. If growth appears on retesting these new ten ampul vials, the entire lot is then reprocessed.

PARENTERAL SOLUTION OF LIVER, 10 U. S. P. UNITS PER CC.-NATIONAL DRUG CO.—A sterile aqueous, clear, dark brown solution containing all of the fraction G of the liver extract (Cohn), preserved with 0.5 per cent of phenol. The daily parenteral administration of 0.1 cc. has been found to produce the standard reticulocyte response defined as 1 U. S. P. unit (injectable) when assayed in cases of pernicious anemia as required by the Council.

Actions and Uses.—Parenteral solution of liver-National Drug Company is proposed for intramuscular injection in the treatment of pernicious anemia. See the general article Liver and Stomach Preparations (New and Nonofficial Remedies, 1940, p. 320).

Dosage.—Daily intramuscular injection of 0.5 cc. for three to four days may be sufficient for the average case. For more severe cases the doses may be raised to from 2 to 4 cc. It is desirable to give at least 20 units (2 cc.) on the first and second days, but it may be advisable in the case of patients who are to receive the larger doses to divide the dose and give one half of the amount into each gluteal muscle. After seven days' interval, 10 units (1.0 cc.) may be administered at weekly intervals. The dosage of course will vary with the individual patient, depending on the degree of complications.

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92. Lewis, A. A., and Turner, C. W.: The Mammogenic Hormones of the Anterior Pituitary: I. The Duct Growth Factor, Research Bulletin 310, University of Missouri College of Agriculture, Agricultural Experiment Station, 1939, pp. 1-72.

93. Lewis, A. A., and Turner, C. W.: Chemical Concentration of Mammogen from Prehypophyseal Tissue, Proc. Soc. Exper. Biol. & Med. 39: 435 (Dec.) 1938.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 28, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.
2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.
3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.
4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.
5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.
6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.
7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.
8. Expansion of public health and medical services consistent with the American system of democracy.

CHANGES IN MAKEUP OF THE JOURNAL

Beginning with the issue for Jan. 4, 1941, the first, third and fourth cover pages of THE JOURNAL will be printed in two colors, utilizing the two color presses just installed. The change is not a radical one, involving only the use of the extra color in order to develop certain features. The general makeup and style of the cover of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION have prevailed for more than forty years and constitute such a well established form that any radical change in the nature of display type, streamlining or similar innovations has not been contemplated. In connection with the use of the additional color, the quality of the paper used for the cover has also been improved, and a finer quality of ink will be utilized.

Consideration was given also to the desirability of changes in the arrangement of the material in the reading pages. For convenience in the handling of the

large amount of material which must now be rushed into THE JOURNAL because of the timeliness of articles dealing with medical preparedness and medical organization, the sections entitled "Book Notices" and "Queries and Minor Notes" have been shifted to a place just previous to the advertising pages in the back of the book. Since much of this material is constantly on hand, it is possible to make up these pages somewhat in advance of the time when the pages dealing with more current material are prepared.

This week's issue of THE JOURNAL is the index number. Readers will find that they have received for a six months period some 2,400 pages of original contributions, editorials, news material, abstracts, answers to questions, reviews of books, medicolegal information and the reports of the various councils of the American Medical Association. THE JOURNAL is proud to say that such a quantity of material of an authoritative, timely and practical character is not made available by any other medical publication in the world, even at twice the price.

THE OPTIMUM POPULATION FOR THE UNITED STATES

The changed complexion of national life which is portended by present trends in population has been discussed frequently by THE JOURNAL.¹ All the evidence of probabilities foreshadows a more or less static population or possibly a slight decrease late in this century, with a shift in age groupings resulting in a larger percentage of the total in the older years and a smaller one of children. This prospect, though contrary to an accustomed pattern, need not give rise to alarm. If, for example, the productive age group is considered to be between the ages of 20 and 65, the percentage of the total population between these ages is sure to increase for another ten years at least and will, even in the event of a slight decrease in total population, remain amply sufficient to support the groups of the population which are dependent on account of age. The percentage in the groups dependent by reason of age may not change much: with an increase in the number of elderly dependents a decrease in the number of children who are dependents is likely to occur. From a careful consideration of the probabilities, Burch² concludes that serious economic problems are not likely to result from this change in proportion of "youngsters" and "oldsters" and that there is little chance of dependent old people controlling the economic and political situation. Those over the age of 65 can never hope to cast more than a quarter of the total vote of the nation, even if no changes are made to restrict their political influence—a possibility with which one must reckon.

1. Headed for the Last Census? editorial, J. A. M. A. 109:1638 (Nov. 13) 1937; Population—Supply and Demand, *ibid.* 109:1726 (Nov. 20) 1937; Changing Population: The Premise, *ibid.* 111:1103 (Sept. 17) 1938; Changing Population: The Inferences, *ibid.* 111:1189 (Sept. 24) 1938.
2. Burch, G. I.: Changing Age Composition of the American People, Population Bulletin, March 1940, Population Reference Bureau, Washington, D. C.

A favorable relationship between the number of people and the natural resources is vital to a democracy, Burch³ believes. Although the unparalleled prosperity which the United States has enjoyed in the past has been closely associated with a rapid increase in population, it should be obvious that its continuation is not dependent on a similar rapid rate of population growth and would indeed even be hindered by a too rapid growth. Recent studies of diet, of land that can be safely cultivated and of this country's capacity to produce and consume have thrown new light on the subject of optimum population for the United States. As pointed out in a study of the Brookings Institute, it would seem that a reasonable minimum aim of our national economy would be to provide the entire population with a liberal diet which would furnish adequate nutrition, a substantial margin of safety in respect to vitamins and minerals, and a satisfying variety of foods. To reach the minimum standards proposed would require an increase in the volume of production over that existing in 1929 of all kinds of consumer goods and service by something like 70 to 80 per cent. In brief, and employing optimistic assumptions which are far removed from existent fact and may not be possible of attainment, it would require a national income of some 146 billion dollars to support 128 million persons at the minimum "optimum" standard of living and assuming an even distribution. However, the population has already exceeded this number (about 132,000,000) and the national income is only about half of the suggested figure. Furthermore, it is almost certain that the population will grow by at least 20 million more by 1980 not including foreign immigration, and even this estimate postulates a decrease of about 25 per cent in the birth rate over the next forty years.

From these studies it may be concluded that the slowing of population growth now manifest is almost certainly a desirable feature in maintaining the superior economic opportunities which place this country in a relatively favorable position as compared with the crowded countries of Europe. The figures also show that there is no need to fear either a lack of available workers or a lack of potential soldiers to meet any threat. Burch⁴ likewise rejects the hypothesis that a high birth rate is a measure of vitality and a low birth rate a measure of national decadence. Economic and social conditions appear to be the real controls of the birth rate and population growth. With the picture of the true meaning of population trends becoming gradually clarified, future emphasis might be placed on quality of the population rather than on quantity alone as measured by the gross number of births. It is at least certain that there will be no shortage of workers or consumers and no overwhelming proportion of dependents in this country in the immediately visible future.

TRAFFIC IN NARCOTIC DRUGS

The U. S. Bureau of Narcotics has recently reported on the traffic in opium and other dangerous drugs for the year ended Dec. 31, 1939.¹ Contained in this report is a most interesting contrast of the prevalence of addiction to narcotic drugs in 1877² and at present. In 1877, according to the report, one in every 400 persons in the United States was addicted to opium or one of its derivatives, while in 1922 and 1938, subsequent to enactment of the Harrison Narcotic Act in 1914, the ratio of such addicts to population was respectively 1 in every 1,000 and 1 in every 3,000. In the state of Michigan in 1877 there were 516 narcotic addicts per hundred thousand of population but in 1938, according to a survey conducted in Michigan by the Bureau of Narcotics in that year, there were only 17 addicts per hundred thousand. Opium or morphine eaters, prevalent in 1877, were not discovered in that survey; most of the addicts used heroin which was highly adulterated. In 1877 this country, with a population of 46,000,000, imported 350,000 pounds of raw opium but during the past few years, since importation of that drug was by law restricted to amounts necessary for medicinal and scientific needs, such imports have averaged only 150,000 pounds yearly for more than 130,000,000 people. In 1877 the average per capita consumption of opium and its derivatives was 53 grains as compared with an average consumption in 1939 of only 8.4891 grains, or 550.091 mg., per capita. The consumption of opium is no longer greatly out of proportion to medical needs. Because the supplies of heroin and morphine, the derivatives of opium commonly used by addicts, are so restricted and the prices so prohibitive, contraband drugs at the time they reach the addict are usually adulterated about 95 per cent. Consequently the average addict today obtains what amounts to less than 1 grain of his drug of addiction daily. Because of the scarcity, dilution or prohibitive price of heroin and morphine, narcotic addicts frequently resort to the use of paregoric, laudanum or the various barbituric acid derivatives. Today there are fewer female than male drug addicts, the ratio being about four males to one female, while in earlier times the reverse was the case owing to the promiscuous use of opiates for the relief of diseases of the female reproductive organs.

In 1877 physicians in many instances were directly responsible for formation of the narcotic habit by patients. Physicians too frequently resorted to the use of narcotic drugs, continued medicines too long, or, which occurred more often, prescribed indiscriminately, so that the patient continued the use of the drug indefinitely. Physicians' prescriptions for narcotic drugs were commonly refilled again and again by druggists.

3. Burch, G. I.: A Study in Optimum Population for the United States, *Population Bulletin*, July 1940.

4. Burch, G. I.: The Birth Rate as a Measure of National Vitality, *Population Bulletin*, April 1940.

1. Anslinger, H. J.: Traffic in Opium and Other Dangerous Drugs for the Year Ended Dec. 31, 1939. U. S. Treasury Department, Bureau of Narcotics, U. S. Government Printing Office, Washington, 1940.

2. Sixth annual report of the Michigan State Board of Health for the fiscal year ended Sept. 30, 1878.

Today, however, the majority of narcotic addicts are of the criminal element and are unknown to physicians and druggists. The medical profession generally is now alive to its responsibilities, and physicians, with the exception of a small minority, are more alert to the dangers surrounding the use of narcotic drugs. The indiscriminate use of narcotic medicines without intelligent medical advice, to which the spread of addiction in 1877 was attributed, is no longer prevalent. Only about 5 per cent of those addicted in 1939 gave this as a reason for their addiction. The Bureau of Narcotics attributes this improved condition in part to the efforts of the American Medical Association in publishing and distributing to the medical profession a book entitled "The Indispensable Use of Narcotics"³ and to better instruction in medical schools. No longer is there frequent dosing of infants with opiates and no longer are family medicine cabinets and nurseries stocked with patented soothing syrups, cordials, anodynes and other preparations containing opium or its derivatives. In 1877 laudanum was a favorite drug of addiction but, to the knowledge of the Bureau of Narcotics, no addict in 1939 acquired his habit originally from the taking of this drug. The creating of an addict during childhood and continuing into the adolescent stage, which was common in 1877, no longer occurs. However, opium, particularly its derivative codeine, is still, and rightly so, the most important drug used by the medical profession.

In 1877 those who had become addicted to opium or its derivatives generally gave as their excuse for acquiring the habit that they had taken their drug of addiction in the beginning to relieve some painful or incurable disease. In 1939, according to the Bureau of Narcotics, over 60 per cent of narcotic addiction was due to association with other addicts. The use of narcotics by prostitutes is still a factor in the narcotic traffic. Narcotic addiction is still formed sometimes when a drunkard resorts to drugs for sobering effects. According to the Uniform Crime Reports for 1939, issued by the Federal Bureau of Investigation of the Department of Justice, the majority of narcotic law violators are major criminals. Of such violators arrested during 1939, 64.6 per cent had previous records and arrests.

A significant problem which still persists is the prescribing or dispensing by a relatively small number of physicians, in violation of the Harrison Narcotic Act, of large quantities of narcotic drugs to addicts, not in the course of bona fide medical treatment but solely to cater to drug addicts and to satisfy their craving for their drug of addiction. During 1939 the Bureau of Narcotics reported to the licensing agencies of the several states, for disciplinary action against physicians, 77 cases of conviction for narcotic irregularities, 62 cases of addiction and 13 cases of conviction or addic-

tion in other states, of which 3 involved unlicensed physicians. During the year, with respect to cases of conviction, the state licensing agencies revoked the physician's license in 21 cases, suspended the physician's license in 4 cases, placed the physician on probation in 15 cases, in 10 of which narcotic privileges were withdrawn, admonished the physician in 1 case, dismissed the case without disciplinary action in 13 cases, and in 5 other cases the physician died before action could be taken. With respect to cases of addiction, the following disciplinary action was taken by the state licensing agencies: revocation of licenses 4, suspension of licenses 4, probations without narcotic privileges 12, probations 10, admonitions 2, dismissed without disciplinary action 20 and in 6 cases the physician died pending action. In the cases of conviction or addiction in other states the state licensing agencies revoked the physician's license in 5 cases, suspended the practitioner's license in 1 case and placed the physician on probation without narcotic privileges in 1 case. On Dec. 31, 1938 the cases pending action before the state licensing boards were 128 cases of conviction, 123 cases of addiction and 17 cases of conviction or addiction in other states, while on Dec. 31, 1939 the cases still pending action numbered 146 cases of conviction, 124 cases of addiction and 21 cases of conviction or addiction in other states. The Bureau of Narcotics calls attention particularly to the failure of one state licensing agency to take any action whatever in 3 cases of conviction of flagrant violation of the Harrison Narcotic Act by physicians in that state which were reported to that agency for disciplinary action. In 1 of those cases the physician issued in one year 996 prescriptions for 52,100 grains of morphine, or 208,400 doses of a quarter grain each.

In the United States the abuse of marihuana (*Cannabis sativa* L.) consists principally in the smoking of the resinous flowering tops and crushed portions of the plant, rolled into cigarettes. The Bureau of Narcotics reports that, since the enactment of the Marihuana Tax Act of 1937, considerable progress has been made toward a solution of this nationwide problem. During the year 1939 federal and state narcotic officers seized 23,289 Kg. 606 Gm. of bulk cannabis, 34 Kg. 841 Gm. of cannabis seeds, 22,567 marihuana cigarettes and approximately 930,880 cannabis plants. Also 9,026 metric tons of cannabis growing on 4,542 hectares of land were eradicated. It is estimated that the total area of uneradicated cannabis growth in this country is approximately 18,211 hectares. During 1939 the Bureau of Narcotics continued its efforts to combat the marihuana smoking practice by preventive educational work, particularly regarding the evils of marihuana. The bureau believes that direct propaganda to youth is undesirable because of the danger of arousing undue curiosity, but that it is desirable for parents, without overemphasis, to educate the youth against the use of marihuana.

3. *The Indispensable Use of Narcotics*, by Various Authors, Chicago, American Medical Association, 1931.

THE JOURNAL commends the enlightened and effective administration of the Bureau of Narcotics. A record such as that here reported indicates effective control. The cooperation of the medical profession has been freely and fully rendered, owing no doubt to recognition by the medical profession of the desire of the bureau to destroy criminal practice without undue interference with the legitimate prescription of narcotic drugs. Complete cooperation with the bureau by state licensing agencies will do much to further this significant work.

Current Comment

PLASMA IN TREATMENT OF ACUTE HEMORRHAGE

The present World War has enormously stimulated studies on effective substitutes for blood transfusion in treatment of hemorrhage. Recently Buttle and his co-workers¹ from the Department of Physiology, Middlesex Hospital, reported an evaluation of various blood substitutes based on controlled experiments in animals. As a result of their work they placed the substitutes in the following order of therapeutic value: (1) plasma, (2) serum, (3) hemoglobin-Ringer, (4) "gum-saline," (5) red cells suspended in "crystalloid" solution, and (6) physiologic solution of sodium chloride or isotonic dextrose solution. By way of practical accord with these conclusions, Aylward and his colleagues² working in Manchester report careful laboratory investigations on the technic of the concentration and drying of plasma. The dried product has several important advantages: stability, economy of storage place, ease of transport, and facility in the preparation of concentrated plasma—the latter arising from the recent recognition that there may be advantages in the use of concentrated plasma which can be readily obtained by dissolving the plasma powder in sterile distilled water to give the required concentration. Any method of drying plasma must fulfil certain conditions, the Manchester investigators point out, namely temperature control, solubility and sterility. Two principal methods of drying are available: the concentration and drying by spray distillation in vacuo, using various types of apparatus, and the concentration and drying of plasma by the cellophane tube method under sterile conditions followed by low temperature drying of the concentrate. Both these methods, they say, enable large amounts of plasma to be concentrated and dried without undue cost. These methods can be applied also to serum. The Manchester workers point out that, while the clinical effects of serum and plasma transfusions are probably similar, there are certain advantages in collecting serum rather than plasma, since serum will dry somewhat more easily than plasma owing to the absence of fibrin, sodium citrate, sodium chloride and possibly dextrose. Additional refinements of technic in the development of

satisfactory and inexpensive methods of preparing blood substitutes are likely to result from the extensive studies now being made in many places.

EFFECT OF CHILDREN ON ECONOMIC STATUS OF AMERICAN FAMILIES

Many factors appear to be involved in the declining birth rate which has been apparent in Western countries for several decades. Lorimer¹ has recently reviewed the economic effect on American families of the appearance of children in various numbers. The most striking change in proportional expenditures in passing from families without children to families with one or more children is in the food item. At given income levels the proportions of the total family expenditures allotted to food rise consistently as the number of children in the family increases. This increased expenditure for food obviously must be offset by curtailment of other expenses. The reduction, however, is not constantly evidenced for any particular group of expenditures but appears at various points, notably household operation, furnishings and equipment, and transportation. In spite of the increased outgo for food, the average food consumption level is actually lowered as the number of children increases. Lorimer points out that if all family types invested an identical proportion of their total income in food, families with three or four children in some areas (Chicago cited specifically) would need just about twice the income of childless families in order to maintain the same consumption levels. Even farm families of several children would need more than 50 per cent larger incomes than childless families of like location. Moreover, the added expenditures for children's clothing are largely offset by reduction in the expenditure of husband and wife for their own clothing. The increased housing needs brought about by children usually result in the acceptance of more crowded quarters or moving to less satisfactory locations. The relation of total expenditure to income, i. e. the margin of savings or liability to debt, also reflects the number of children in a family. The degree of the economic effect of children varies with the income level and it influences and is influenced by the gainful employment of both parents. Indeed the entire economic outlook and practice are fundamentally involved by the addition of children to the family. Intelligent population policy requires that attention be given to these conditions. Lorimer believes it essential that some aid and support to families be established so that parents need not as at present jeopardize the standards of living which they set for themselves and their children if they wish to add new lives to the family. There are two possible approaches to equalization of levels of living among families with none or few children and large families: the family allowance proportionate to the number of children and the system of special service and subsidy to families with children along the lines developed in Sweden. In the problems which these facts present, policies concerned with population are paramount and require further research, experimentation and public attention.

1. Buttle, G. A. H.; Kekwick, Alan, and Schweitzer, A.: Blood Substitutes in Treatment of Acute Hemorrhage, *Lancet* 2: 507 (Oct. 26) 1940.

2. Aylward, F. X.; Mainwaring, B. R. S., and Wilkinson, J. F.: The Concentration and Drying of Plasma, *Brit. M. J.* 2: 4165 (Nov. 2) 1940.

1. Lorimer, Frank: The Effect of Children on the Economic Status of American Families, *J. Heredity* 31: 300 (June) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

COMMITTEE ON AVIATION MEDICINE INSPECTS FACILITIES

Members of the committee on aviation medicine of the National Research Council recently made a tour of aviation medical facilities of the United States, Canada and Cuba. The group included Drs. Eugene F. Du Bois, New York, chairman of the committee; Cecil K. Drinker, Boston; John F. Fulton, New Haven, Conn.; Eugene M. Landis, Charlottesville, Va. They were accompanied by Comdr. J. F. Poppen of the U. S. Navy and Capt. Lloyd Griffis, U. S. Army. The facilities visited included Wright Field, Dayton, Ohio; the Naval Base at San Diego, Calif.; Guantanamo, Cuba, and the University of Toronto in Canada.

CIVILIANS AND HOSTILE AIRCRAFT

Dr. Gustave E. Ledorf, captain, Medical Corps, the Army Industrial College, Washington, D. C., gave a public lecture in Rochester, N. Y., December 1, under the sponsorship of the Rochester Academy of Medicine, the Medical Society of the County of Monroe and the University of Rochester School of Medicine. His subject was "Care of the Civilian Population Necessitated by Hostile Aircraft."

SARANAC LAKE MEDICAL SOCIETY

The Saranac Medical Society, Saranac Lake, N. Y., at a meeting in the Saranac Laboratory, November 13, adopted a resolution recommending that all men entering the army services receive a roentgen examination of the chest before induction into the service. The guest

speakers at this meeting were Drs. S. F. Marshall and E. D. Kiefer of the Lahey Clinic, Boston, and their subject was "Medical-Surgical Treatment of Peptic Ulcer."

FIVE NEW BRIGADIER GENERALS

Five colonels of the U. S. Army Medical Department have been promoted to temporary Brigadier Generals as of October 1, according to the *Military Surgeon*. They are Brig. Gen. Albert G. Love, who will remain on duty as chief of the planning and training division in the Surgeon General's Office; Wallace DeWitt, now at Letterman General Hospital, Presidio of San Francisco; William L. Sheep, who is to be commanding general of the new army general hospital to be established in the vicinity of Atlanta, Ga.; Morrison C. Stayer, chief medical officer of the Panama Canal, and Howard McC. Snyder, who has been detailed in the Inspector General's Department.

FIELD HOSPITAL SENT TO ENGLAND

The American Field Hospital Corps has presented to the British War Relief Society a mobile field hospital of forty-one units, twenty-five trucks and trailers and sixteen weather-proof tents. The hospital, valued at \$100,000, is equipped to accommodate 100 bed patients and a hospital staff of fifty. It is completely self contained and can be operated in devastated and isolated districts where shelter, power and other facilities for taking care of epidemics and the critically injured do not exist, according to the *New York Times*. The unit was taken to Staten Island, December 15, for shipment to England.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY WAR DEPARTMENT

The following additional medical reserve corps officers had been ordered to extended active duty with the regular army by direction of the War Department, Washington, D. C., up to December 13:

BELISLE, John Alexander, 1st Lieut., Mount Clemens, Mich.
CHASEN, William Henry, 1st Lieut., Brooklyn.
DALY, Joseph Michael, 1st Lieut., Laurel, Md.
EVANS, Charles Welton, Jr., 1st Lieut., Fastrill, Texas.

EWAN, John Radcliffe, 1st Lieut., Philadelphia.
GALIN, Jack, 1st Lieut., Jacksonville, Fla.
GILES, Robert W., 1st Lieut., Arkansas Pass, Texas.
GOODMAN, Eli, 1st Lieut., Chicago.
HAIMES, Solomon Manuel, 1st Lieut., Allentown, Pa.
LEVIN, Emanuel Jack, 1st Lieut., Philadelphia.
LOOMER, Harry Pincus, 1st Lieut., Brooklyn.
NICHOLS, Ace Elliott, 1st Lieut., Corpus Christi, Texas.
THOMASSY, George Ernest, 1st Lieut., Washington, D. C.
TOLOFF, Edward Myron, 1st Lieut., Pittsburgh.

FIRST CORPS AREA

The following additional medical reserve officers had been ordered to extended active duty with the regular army by the Commanding General, First Corps Area, up to December 6. The First Corps Area comprises the states of Maine, Vermont, New Hampshire, Rhode Island, Massachusetts and Connecticut.

ABRAMS, Herbert, Lieut., Lowell, Mass.
ALPERT, Max, Lieut., Bridgeport, Conn.
ANGELO, Peter, Lieut., Allston, Mass.
BERMAN, Bernard A., Lieut., Waterbury, Conn.
COYNE, Arthur A., Captain, Northampton, Mass.

HENDERSON, John W., Captain, Worcester, Mass.
HOWARD, James H., Lieut., Pittsfield, Mass.
JOSLIN, Allen P., Lieut., Boston.
MEISTER, Abraham J., Lieut., Lawrence, Mass.
PAGLIARO, Joseph J., Lieut., Derby, Conn.
PHILLIPS, Robert T., Captain, Portland, Maine.
ROSEN, Abraham E., Lieut., Bangor, Maine.
ROZEN, Alan A., Lieut., New Haven, Conn.
SEGEL, Arnold L., Lieut., Boston.
SIMARD, Louis Basil, 1st Lieut., Haverhill, Mass.
STEWART, Artemas J., Captain, Lowell, Mass.
THOMPSON, Bob F., Lieut., New Haven, Conn.
WESOLY, Andrew S., Lieut., New Britain, Conn.
WILLARD, Paul C., Lieut., Montpelier, Vt.
WITTIG, Joseph E., Lieut., West Warwick, R. I.

SECOND CORPS AREA

The following additional medical reserve officers had been ordered to active duty by the Commanding General, Second Corps Area, up to December 13. The Second Corps Area comprises the states of New York, New Jersey and Delaware.

ALEXANDER, Stewart F., 1st Lieut., Park Ridge, N. J.
AMDUR, Marvin L., 1st Lieut., Buffalo, 1st Military Area.
ANGELO, Martin A., 1st Lieut., Buffalo, 1st Military Area.
BABBITT, Hugh M., 1st Lieut., Plainfield, N. J., 3d Military Area.
BACKER, Max B., 1st Lieut., Brooklyn, 2d Military Area.
BARONE, Francis A., 1st Lieut., Jersey City, N. J., 3d Military Area.
BERGSTEIN, Joseph, Captain, Brooklyn, 2d Military Area.
BEYER, William, Major, Edgewater, N. J., 3d Military Area.
BLOOM, Bernard B., 1st Lieut., Brooklyn, 2d Military Area.
CHAMPLIN, Ray D., Lieut. Col., Oneonta, N. Y., 1st Military Area.
CHURCH, Sheldon, 1st Lieut., Albany, 1st Military Area.
DEIBERT, Kirk R., 1st Lieut., Woodllynne, N. J.
DESERVO, Thomas G., 1st Lieut., New York, 2d Military Area.
DOLTOLO, Joseph J., 1st Lieut., Poughkeepsie, N. Y.
ENGEL, Edward F., Captain, Seneca Falls, N. Y., 1st Military Area.
EUPHRAT, Edwin J., 1st Lieut., Flushing, N. Y.
FEINGOLD, Abraham, 1st Lieut., Brooklyn.
FORD, William G., 1st Lieut., Buffalo, 1st Military Area.
FRANK, Simon C., 1st Lieut., Williston, N. Y., 2d Military Area.
FRED, Leo, 1st Lieut., Brooklyn, 2d Military Area.
FREEMAN, Nathan, Captain, 1236 Pacific Street, Brooklyn.
GILLIS, Alfred G., Captain, Clayton, N. J., 3d Military Area.
GLENN, James A., Jr., 1st Lieut., North Creek, N. Y., 1st Military Area.
GOLDBERG, Irwin, 1st Lieut., New York, 2d Military Area.
GREENE, John E., 1st Lieut., Jamaica, N. Y.
HOFFMAN, Floyd W., 1st Lieut., Romulus, N. Y.
HOLLEY, Emerson, 1st Lieut., Lockport, N. Y., 1st Military Area.
HOWLAND, Reeve S., 1st Lieut., Elmira, N. Y., 1st Military Area.
KIVEN, Nathan J., 1st Lieut., Jamaica, N. Y., 2d Military Area.
MARKULIS, Emil J., 1st Lieut., Orchard Park, N. Y., 1st Military Area.
MARSHALL, Irving, 1st Lieut., Jersey City, N. J., 3d Military Area.

McGOWAN, John F., 1st Lieut., Buffalo, 1st Military Area.
MEISTER, Peter C., 1st Lieut., Buffalo, 1st Military Area.
MENDEN, Julian, Captain, New York.
MESSINA, John L., 1st Lieut., Brooklyn, 2d Military Area.
MORCHAN, Samuel, 1st Lieut., Angelica, N. Y., 1st Military Area.
NADLER, Arthur A., Captain, Plainfield, N. J., 3d Military Area.
NEDELL, Ralph S., 1st Lieut., Brooklyn.
O'TOOLE, John S., Jr., 1st Lieut., Potsdam, N. Y., 1st Military Area.
PATTI, Samuel R., 1st Lieut., Dunkirk, N. Y., 1st Military Area.
RITTER, Fred L., Major, Syracuse, N. Y., 1st Military Area.
ROACH, John S., 1st Lieut., Medina, N. Y., 1st Military Area.
SABIN, Anthony G., Captain, New York, 2d Military Area.
SAYER, John W., 1st Lieut., Gouverneur, N. Y., 1st Military Area.
SCHOEDEL, Adrian C., 1st Lieut., Flushing, N. Y., 2d Military Area.
SCHWARTZ, Leon J., 1st Lieut., Greenwich, N. J.
SHAEN, Edward, 1st Lieut., Camden, N. J.
STERN, Leon B., 1st Lieut., New York, 2d Military Area.
STOLA, Augustus G., 1st Lieut., New York, 2d Military Area.
TINKER, Martin B., Jr., 1st Lieut., Ithaca, N. Y., 1st Military Area.
SMUDA, Alphonse C., 1st Lieut., Glendora, N. J.
SOMMER, George N. J., Jr., 1st Lieut., Trenton, N. J.
SULLIVAN, Norbert P., Captain, Jackson Heights, N. Y., 2d Military Area.
TEGMEYER, Charles E., 1st Lieut., Hamilton, N. Y.
WEISS, Mortimer, 1st Lieut., Hudson Falls, N. Y., 1st Military Area.
WELGE, Carl J., 1st Lieut., Roosevelt, N. Y., 2d Military Area.

Orders Not Issued

Medical reserve officers reported in THE JOURNAL, Nov. 16, 1940, page 1727, as having been ordered to active duty but whose orders have not been issued:

CREIGHTON, James J., 1st Lieut., Buffalo.
DURHAM, James R., Jr., 1st Lieut., Wilmington, Del.
HAYMAN, Charles R., 1st Lieut., Scarsdale, N. Y.
KARPEL, Bernard, 1st Lieut., New York.
KURLAND, Harry A., 1st Lieut., New York.

FOURTH CORPS AREA

The following additional medical reserve officers had been ordered to active duty by the Commanding General, Fourth Corps Area, up to December 6. The Fourth Corps Area comprises the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana:

ANDERSON, Henry L., 1st Lieut., Sellers, Ala.
BELL, Kenneth R., Captain, Sanford, Fla.
BENTON, Wayne J., 1st Lieut., Greensboro, N. C.
BERRY, Robert L., Jr., 1st Lieut., Villa Rica, Ga.
BISHOP, Louis D., 1st Lieut., DeQuincy, La.
BOOZER, Thomas S., 1st Lieut., Talladega, Ala.
BROWN, Stephen W., 1st Lieut., Milledgeville, Ga.
CLAPP, Hubert L., 1st Lieut., Swannanoa, N. C.
COGDILL, David M., 1st Lieut., Fayetteville, N. C.
CORNELL, William S., Captain, Charlotte, N. C.
DENHOLM, John S., 1st Lieut., Burlington, N. C.
DISMUKES, Jackson B., Captain, Haines City, Fla.
DOTSON, Walter S., Jr., 1st Lieut., Westmoreland, Tenn.
EDWARDS, William W., 1st Lieut., Greenville, S. C.
EVERS, Herbert R., 1st Lieut., Andalusia, Ala.
EXLEY, David W., 1st Lieut., Miami Beach, Fla.
FARMER, William A., 1st Lieut., Fayetteville, N. C.
GORDON, Joseph T., 1st Lieut., Pulaski, Tenn.
GRIFFIN, Louie H., 1st Lieut., Gibson, Ga.
GRIFFIN, Taylor W., 1st Lieut., Quincy, Fla.
HATFIELD, John R., 1st Lieut., Orlando, Fla.
HAY, Floyd B., 1st Lieut., Byrdstown, Tenn.
HEUER, Douglas F., Jr., 1st Lieut., Memphis, Tenn.
HIGHTOWER, Jesse R., 1st Lieut., Itta Bena, Miss.
JACOB, Harold J., 1st Lieut., Columbus, Miss.
KING, Lebbey B., 1st Lieut., Lake City, S. C.
LUSTGARTEN, Jack G., 1st Lieut., Buxton, N. C.
LYNN, Cy K., 1st Lieut., Valdese, N. C.
McMANUS, Hugh F., 1st Lieut., Raleigh, N. C.
MARTIN, Carl T., 1st Lieut., Haleyville, Ala.

MILLER, Edward S., 1st Lieut., Murphy, N. C.
MOORE, Haywood L., 1st Lieut., Porterdale, Ga.
NUNGESTER, Garrold H., 1st Lieut., Decatur, Ala.
ODEN, Lewis H., Jr., 1st Lieut., Blackshear, Ga.
PALMER, Yates S., 1st Lieut., Valdese, N. C.
PARKER, Shepherd F., 1st Lieut., Shelby, N. C.
PATTON, Marion L., Captain, Memphis, Tenn.
PEASLEY, Elmus D., Major, Raleigh, N. C.
PENTECOST, Ben L., 1st Lieut., Memphis, Tenn.
QUILLIAN, William B., Jr., 1st Lieut., Cartersville, Ga.
ROBERTSON, Carroll B., 1st Lieut., Jackson, N. C.
ROBBINS, Eric P., 1st Lieut., Brockhaven, Miss.
RUSSELL, Alexander B., 1st Lieut., Winder, Ga.
RUSSELL, Ralph E., 1st Lieut., Ocala, Fla.
RUSSELL, Ralph S., 1st Lieut., Ocala, Fla.
SCHUESSLER, George D., Captain, Columbus, Ga.
SEGERSON, Edward C., 1st Lieut., Memphis, Tenn.
SHAW, Clarence, 1st Lieut., Chattanooga, Tenn.
SMAHA, Tofey G., 1st Lieut., Griffin, Ga.
SMITH, John E., 1st Lieut., Fitzgerald, Ga.
SMITH, Virgil D., 1st Lieut., Leeds, Ala.
SYKES, Charlie L., 1st Lieut., Pilot Mountain, N. C.
WACHTEL, Leo M., Jr., 1st Lieut., Jacksonville, Fla.
WEEKS, Richard B., Captain, Augusta, Ga.
WELLING, Arthur W., 1st Lieut., Newberry, S. C.
WILLIAMS, Miles W., 1st Lieut., Gamilla, Ga.
WORTHY, William S., 1st Lieut., Carrollton, Ga.
YEOMANS, James W., 1st Lieut., Barnesville, Ga.
ZIRKLE, John G., 1st Lieut., Greeneville, Tenn.

Relieved from Duty

The following officers previously reported have been relieved from duty, or the orders have been revoked:

JORDAN, William K., 1st Lieut., Milledgeville, Ga.
MUSE, William S., 1st Lieut., Knoxville, Tenn.

SEVENTH CORPS AREA

Ordered to Camp Joseph T. Robinson

The following medical reserve corps officers had been ordered to extended active duty by the Commanding General, Seventh Corps Area, up to December 13, with permanent station at Camp Joseph T. Robinson, Arkansas. The Seventh Corps Area comprises the states of North Dakota, South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri, Arkansas and Wyoming.

BROWN, James Matthews, 1st Lieut., Caledonia, Minn.
BURTON, Frank Marques, 1st Lieut., Hot Springs National Park, Ark.
CLARK, Henry Bannister, Jr., Captain, St. Paul.
DALEY, Lyle Miner, Major, Hamilton, Mo.
DEVINE, John Leo, Jr., 1st Lieut., Minot, N. D.
DUNLAP, Richard Leonidas, 1st Lieut., Lawrence, Kan.

HAIGLER, James Pierre, 1st Lieut., Pittsburg, Kan.
HARRISON, Glenn Ellwood, Captain, Mason City, Iowa.
HENDERSON, Robert Wesley, Captain, Bismarck, N. D.
HOBBS, Russell Eugene, 1st Lieut., Wichita, Kan.
HOGAN, Paul Wilbur, Captain, Waukon, Iowa.
JOHNSTON, Charles Harlan, Captain, Des Moines, Iowa.
LENTZ, Harold Calvin, 1st Lieut., Neosho, Mo.
MASON, James Anders, 1st Lieut., International Falls, Minn.
MEYER, Alvin John, Captain, Lake City, Minn.
NEWKIRK, William Henry, Captain, Berryville, Ark.
PATTERSON, Harold Loyd, 1st Lieut., Lyons, Kan.
RIEGLMAN, Ralph Harold, 1st Lieut., Des Moines, Iowa.
SCHERLING, Sidney Saul, Captain, Taylors Falls, Minn.
SIEBERT, Norman Clifford, 1st Lieut., Canada, Kan.
STEINLE, George Henry, Captain, Burlington, Iowa.
STERNHILL, Irving, Captain, Mason City, Iowa.
TONEY, William Egbert, 1st Lieut., St. Joseph, Mo.
WEBSTER, LuVerne John, 1st Lieut., Battle Lake, Minn.
WILSON, William Errol, 1st Lieut., Greensburg, Kan.

The following officers are ordered to extended active duty for a period of one year with permanent station at Fort Snelling, Minnesota:

JOHNSON, Christian G., 1st Lieut., Rugby, N. D.
McCANN, Eugene John, Captain, Minneapolis.

The following officer is ordered to extended active duty for a period of one year with permanent station

at Jefferson Barracks, Missouri, by the Commanding General, Seventh Corps Area:

SCHUCK, Carl Alfred, Captain, St. Louis.

The following officer is ordered to extended active duty for a period of one year with permanent station at Fort Meade, South Dakota:

NYQUIST, Roy Henning, Captain, Iroquois, S. D.

EIGHTH CORPS AREA

The following additional medical reserve officers had been ordered to active duty by the Commanding General, Eighth Corps Area, up to December 13. The Eighth Corps Area comprises the states of Colorado, Arizona, New Mexico, Oklahoma and Texas.

AARNI, John C., 1st Lieut., Hayden, Ariz.
BAGGETT, Seldon O., 1st Lieut., Austin, Texas.
BALDRIDGE, Max, 1st Lieut., Bowie, Texas.
BUKOWSKI, Lucian M., Captain, Houston, Texas.
BURNETT, Berry H., Lieut. Col., Englewood, Colo.
CANTRELL, William B., Lieut. Col., Gallup, N. M.
COCHRAN, Joel L., Major, San Antonio, Texas.
COHEN, Mayer, 1st Lieut., Marlin, Texas.
COOLEY, Ben H., Major, Norman, Okla.
DARNELL, Elmer E., Major, Colony, Okla.
DAVIS, Charles Q., Major, Houston, Texas.
DAVIS, James H., Lieut. Col., Fort Worth, Texas.
FULMER, H. Ray, 1st Lieut., Ringling, Okla.
GALLAHER, Frank C., 1st Lieut., Shawnee, Okla.
GEE, Kenneth J., 1st Lieut., Tulsa, Texas.
GWINN, Frank W., Captain, Yuma, Ariz.
HARRELL, Fred S., Captain, Olney, Texas.
HAWKINS, Winfred W., Captain, Waco, Texas.
HOLTZ, Harvey E., 1st Lieut., Dallas, Texas.
JOHNSON, George H., Major, Ardmore, Okla.
KEATING, Peter M., Lieut. Col., San Antonio, Texas.
KINDER, Thurman A., Major, Brownsville, Texas.
LAPAN, Charles H., 1st Lieut., Lamar, Colo.

LEHMANN, Cornelius F., Major, San Antonio, Texas.
LITTELL, George S., Major, Dallas, Texas.
LOWIN, Julian R., 1st Lieut., Redvale, Colo.
LUBBEN, John F., Jr., Major, Dallas, Texas.
MAGID, Morston A., 1st Lieut., Denver.
MILES, John B., Captain, Anadarko, Okla.
MOORE, Isham Seller, 1st Lieut., Ozono, Texas.
MOORE, John D., Major, Fort Worth, Texas.
MURRAY, Edward Cotter, Captain, Ada, Okla.
NICHOLSON, John R., Major, San Antonio, Texas.
OLIVER, Claudius H., Lieut. Col., Douglas, Ariz.
PACE, Bedford F., 1st Lieut., Noderland, Texas.
POLLACK, Simon, 1st Lieut., Tulsa, Okla.
PRIDAY, Codric, Major, Corpus Christi, Texas.
PROSSER, Moorman P., 1st Lieut., Norman, Okla.
RAGAN, Tillman A., 1st Lieut., Fairfax, Okla.
ROBERTS, Charles J., 1st Lieut., Enid, Okla.
SAKS, Harry S., Captain, Denver.
SANFORD, Herbert M., 1st Lieut., Perryton, Texas.
SHAW, Dwight B., Captain, Pueblo, Colo.
SHORBE, Howard B., 1st Lieut., Oklahoma City.
SLAY, Iris J., Major, Fostoria, Texas.
STUARD, Charles G., Jr., 1st Lieut., Tulsa, Okla.
WALKER, Marcellus A., Jr., Captain, Paris, Texas.
WINTER, John W., Captain, San Antonio, Texas.
WOLF, Edward T., Major, Houston, Texas.

Orders Revoked

KERNEK, Paul, 1st Lieut., Oklahoma City.
TURNBOW, William Ray, 1st Lieut., Tulsa, Okla.

NAVAL RESERVE OFFICERS ORDERED TO ACTIVE DUTY

The following additional naval medical reserve officers have been ordered to active duty:

BARNES, Mark H., Lieut., M. C.-V. (S.), New York, Submarine Base, New London, Conn.
EHRlich, Harry, Lieut. (j. g.) M. C.-V. (G.), U. S. N. R., Dispensary, Navy Yard, Brooklyn.
HARRISON, Edward K., Lieut., M. C.-V. (S.), U. S. N. R., Ossining, N. Y., Ossining Hospital, Marine Barracks, Quantico, Va.
HELD, Albert H., Lieut., M. C.-V. (G.), Huntingburg, Ind., Norfolk Naval Hospital, Portsmouth, Va.
HIGGINS, Homer A., Comdr., M. C.-V. (S.), Little Rock, Ark., to Director of Selective Service, Arkansas (Duty as State Medical Adviser).
HOEY, Waldo O., Lieut., M. C.-V. (S.), Providence, R. I., Naval Training Station, Newport, R. I.
HORST, John V., Lieut., M. C.-V. (S.), Upper Arlington, Ohio, Naval Hospital, Great Lakes, Ill.
HOYLE, Christian K. C., Lieut., M. C.-V. (S.), Roanoke, Va., Jefferson Hospital, First Marine Brigade, Fleet Marine Force, Quantico, Va.
KEIGWIN, Charles G., Lieut. (j. g.) M. C.-V. (S.), Evanston, Ill., Naval Reserve Aviation Base, Chicago.

KING, W. Ivan, Lieut. Comdr., M. C.-V. (S.), Dallas, Texas, Hospital, San Diego, Calif.
LETCHER, Charles W., Lieut., M. C.-V. (S.), Wilkes Barre, Pa., Naval Reserve Aviation Base, Philadelphia.
LEVY, Louis K., Jr., Lieut. (j. g.) M. C.-V. (S.), New Orleans, Marine Recruiting Station, New Orleans.
MARCO, David M., Lieut., M. C.-V. (S.), Amarillo, Texas, Naval Air Station, Jacksonville, Fla.
MILLER, Wade Hampton, Lieut. Comdr., M. C.-V. (G.), Kansas City, Mo., Naval Reserve Aviation Base, Kansas City, Kan.
MORRISON, Arlo A., Lieut., M. C.-V. (S.), Santa Barbara, Calif., Naval Hospital, San Diego, Calif.
OARD, Harry Clifford, Lieut. Comdr., M. C.-V. (S.), Jamaica, N. Y., Norfolk Naval Hospital, Portsmouth, Va.
SIMPSON, George W., Jr., Lieut., M. C.-V. (S.), Norfolk, Va., Navy Yard Dispensary, Norfolk Navy Yard, Portsmouth, Va.
WALVOORD, James H., Lieut. Comdr., M. C.-V. (S.), Hollis, N. Y., Norfolk Naval Hospital, Portsmouth, Va.
WRIGHT, Orville M., Lieut. (j. g.) M. C.-V. (G.), Nashville, Tenn., Vanderbilt University Hospital, Navy Recruiting Station, Nashville, Tenn.

AVIATION MEDICAL EXAMINERS

The following medical officers of the U. S. Army, who have been under instruction at the School of Aviation Medicine, Randolph Field, Texas, graduated as Aviation Medical Examiners, October 19:

ANDERSON, John L., Captain, M. Res., Barksdale Field, La.
BARRETT, Robert S., 1st Lieut., M. C. R., Langley Field, Va.
BILOTTA, Laurence A., Captain, M. C., Army Medical Center, Washington, D. C.
BLOUNT, Robert H., Captain, M. C., Vancouver Barracks, Wash.
BROOKS, Robert H., M. C. R., Kelly Field, Texas.
CALAWAY, William, Captain, M. C., Army Medical Center, Washington, D. C.
CAMERON, Richard R., Captain, M. C., Army Medical Center, Washington, D. C.
CROUCH, Thomas H., 1st Lieut., M. C., Fort Bliss, Texas.
DIAMOND, Max M., M. C. R., Kelly Field, Texas.
GARCIA, Charles Todd, 1st Lieut., M. C. R., Puerto Rican Department.
HARGAN, William S., Captain, M. C., Fort Benning, Ga.
JENKINS, Raymond T., Captain, M. C., Fort Bragg, N. C.

JOHNSON, Hensley S., Captain, M. C., AC Advanced Flying School, San Angelo, Texas.
KELLY, Frederick C., Captain, M. C., AC Advanced Flying School, San Angelo, Texas.
LELICH, Bronko P., 1st Lieut., M. C., Army Medical Center, Washington, D. C.
LLOYD, Harvey L., Captain, M. C., Army Medical Center, Washington, D. C.
MARKS, Maurice Isaac, 1st Lieut., M. C. R., Maxwell Field, Ala.
MATTHEWS, John L., Captain, M. C., Texas National Guard, San Antonio, Texas.
McDONOUGH, Joseph F., 1st Lieut., M. C. R., Moffett Field, Calif.
McGREGG, George D., Captain, M. C., AC Basic Flying School, Montgomery, Ala.
MORRIS, Charles K., Captain, M. C., Westover Field, Chicopee Falls, Mass.
PERRI, Frank A., 1st Lieut., Langley, Field, Va.
PIGFORD, Charles Alfred, Captain, M. Res., Maxwell Field, Ala.
SHAFFER, Frank J., 1st Lieut., M. C., AC Troops, Savannah, Ga.
SOLTZ, Gustav D., 1st Lieut., M. C. R., Lowry Field, Denver.
STAFFORD, Charles A., 1st Lieut., M. C., Fort Douglas, Utah.
TALBOT, John M., Captain, M. C., Hamilton Field, Calif.
TOWNER, Alonzo A., Jr., Captain, M. C., Fort George Wright, Wash.
WAINER, Amos S., 1st Lieut., Randolph Field, Texas.

ORGANIZATION SECTION

OFFICIAL NOTES

THE CLEVELAND SESSION

Special Exhibits on Fractures and on Lame Backs

The Committee on Scientific Exhibit announces that there will be two special exhibits at the Cleveland session as follows:

Special Exhibit on Fractures.—Presented by a committee composed of Dr. Kellogg Speed, Chicago, chairman; Dr. Frank D. Dickson, Kansas City, Mo., and Dr. Walter Estell Lee, Philadelphia.

Special Exhibit on Lame Backs.—Presented under the auspices of a committee composed of Dr. Frank R. Ober, Boston, chairman; Dr. Carl E. Badgley, Ann Arbor, Mich.; Dr. J. Archer O'Reilly, St. Louis; Dr. Arthur Steindler, Iowa City, and Dr. Philip D. Wilson, New York.

Applications for space for other exhibits close on Jan. 20, 1941. Blanks may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

RADIO BROADCASTS

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs being presented by the American Medical Association and the National Broadcasting Company.

The series opened Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the A. M. A. meeting at Cleveland on June 4, 1941. The program is scheduled for 10:30 p. m. eastern standard time (9:30 central, 8:30 mountain, 7:30 Pacific time) over the Blue network, other N. B. C. stations and Canadian stations.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio

network and local stations, and no revenue is derived from the programs. Therefore, local stations may or may not take the programs, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

Some radio stations may be unable to broadcast the program at the regular scheduled time and may transcribe and broadcast it at another hour or even on another day. It is advisable, therefore, to verify the time by reference to local newspapers or by telephoning the local Blue network stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in *THE JOURNAL* and monthly in *Hygeia*, The Health Magazine.

Tickets are available for each broadcast. Address the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Tickets are free, but a stamped self-addressed envelop should accompany requests.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

January 1.* Otorhinolaryngologist.
January 8. Your Eyes.
January 12. Best Foot Forward.

* This program only will be broadcast one hour and a half earlier than the regular scheduled time in order to clear the network for international broadcasts later in the evening.

WOMAN'S AUXILIARY

National Board Meeting

The stated meeting of the board of directors of the Woman's Auxiliary to the American Medical Association was held, November 29, in Chicago with Mrs. V. E. Holcombe, Charleston, W. Va., the president, presiding.

The four past national presidents who attended were Mrs. Samuel Clark Red, Houston, Texas; Mrs. Rogers N. Herbert, Nashville, Tenn.; Mrs. Robert E. Fitzgerald, Milwaukee, and Mrs. Charles C. Tomlinson, Omaha. Mrs. R. E. Mosiman, Seattle, president-elect, was present, as were also ten members of the executive committee, ten chairmen of standing committees, sixteen state presidents, three state presidents-elect and four regional chairmen. Mr. Frank V. Cargill and Dr. W. W. Bauer were guest speakers, answering questions on *Hygeia* and the A. M. A. radio hour series respectively. Four members of the Advisory Council, Drs. Booth, Bloss, Fenton and Sensenich and Dr. Van Etten, President of the American Medical Association, were guests at lunch. Mrs. Red, first president of the national auxiliary, was guest of honor. Twelve visiting Chicago auxiliary women were also present. The nominating committee was elected and plans were made for the convention in Cleveland, June 1-6, 1941.

Preceding the board meeting, the advisory council was host at the A. M. A. headquarters at a luncheon for the executive committee of the auxiliary. Many enjoyed the opportunity of making a tour of the American Medical Association Building.

California

The auxiliary to the Los Angeles County Medical Association gave a formal dinner-dance November 5 at the Wilshire Bowl for the benefit of the Los Angeles Physicians' Aid Association. A sum of \$500 was realized from the affair, which, it is planned, will be held annually for the same purpose.

Nebraska

The auxiliary to the Lancaster County Medical Society met, Nov. 4, 1940, at the home of Mrs. Wesley Becker. Mrs. A. D. Brown, state president, was a guest and spoke briefly. Mr. M. C. Smith, executive secretary to the Nebraska State Medical Association, talked to the group on medical legislation.

The Adams County Medical Association and its woman's auxiliary met for a dinner meeting at Ingleside, Nov. 6, 1940. Judge Blackledge, the after-dinner speaker, spoke on "The Story of a Witness." The auxiliary is knitting and crocheting for the Red Cross.

The officers of the six-county medical auxiliary were entertained at a luncheon, October 9, at the Perkins Hotel in David City by Mrs. R. C. Gramlich, president. Mrs. A. D. Brown was an honor guest.

Utah

The Woman's Auxiliary to the Salt Lake County Medical Society met in October at the Newhouse Hotel to discuss "Where Go the Boats," and folk lore of all nations. The afternoon was in charge of Mrs. Walter H. Horton, who, in rhyme, introduced the speakers—Mrs. L. A. Stevenson, Mrs. Richard P. Middleton, Mrs. J. Albert Peterson and Mrs. Francis Boyer. Music featuring Indian and Chinese melodies was played by Mrs. Claude L. Shields. Preceding the regular program a pageant, "Hygeia, Goddess of Health," was given by Mrs. Alfred Clawson, Mrs. Raymond Maw and Mrs. Roland Merrill. Tea and a social hour followed the program.

A business meeting of the Utah County auxiliary was held in October at the home of Mrs. Garland Pace in Provo. Mrs. Wilford Woolf, the president, was in charge of the meeting.

The state board, with Mrs. J. R. Morrell of Ogden presiding, held its meeting in October at the Lion House in Salt Lake City. Plans for the year were outlined.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

Personal.—Dr. Edward F. Ellis, Fayetteville, has given his medical library of more than 1,000 volumes to the University of Arkansas School of Medicine, Little Rock.—Dr. John L. Ruff, formerly of St. Paul, has been appointed medical director for Crawford, Franklin and Logan counties, succeeding Dr. Albert S. J. Clarke, Ozark, who plans to enter the school of public health at Harvard University, it is reported.—Dr. James M. Lemons, Pine Bluff, has given his medical library to the Jefferson County Medical Society.

CALIFORNIA

Outbreak of Influenza.—A report has been received concerning the recent epidemic of influenza in San Francisco. According to Dr. Jacob C. Geiger, city health officer, the disease appeared in mild form. The incubation period ranged from three to five days and was even as short as twenty-four hours. It is estimated that 10 per cent of the population in the city was affected.

Society News.—The Los Angeles Society of Neurology and Psychiatry and the Endocrine Study Group held a joint meeting, December 18; a symposium on the hypothalamus was presented by Drs. Cyril B. Courville, Samuel J. Glass, Frederick S. Modern and Arthur R. Timme.—The speakers before the Los Angeles Society of Ophthalmology and Otolaryngology, December 23, included Drs. Daniel E. Ziskin on "Destructive Ophthalmia Associated with Atypical Erythema Multiforme," and Warren A. Wilson, "Congenital Lenticule Fibroblastic Membranes."

CONNECTICUT

Fatality from Tularemia.—The death of a man at the Newington Hospital, East Hampton, December 14, from tularemia is said to be the first from this cause in the state, according to the *New York Times*. The man cut his finger while preparing a rabbit, which he had killed on a hunting trip November 23. Five days later he showed symptoms. He became unconscious and was taken to the hospital December 9.

Course on Industrial Medicine.—The Connecticut Clinical Congress has arranged a course on industrial medicine for physicians of the state to begin January 9 at Yale University School of Medicine, New Haven. The first subject will be "Ventilation in Industry." Other subjects to be discussed are:

- January 16, Pulmonary Diseases Due to Dust.
- January 23, Infections in Industry.
- January 30, Dermatitis and Carcinogenic Substances.
- February 6, Poisoning by Benzol—Other Industrial Solvents.
- February 13, Carbon Monoxide Poisoning and Other Irritant Gases.
- February 20, Lead Poisoning.
- February 27, Poisoning by Other Heavy Metals.
- March 6, Caisson Disease and Diseases Due to Changes in Atmospheric Pressure.
- March 13, Cardiac Diseases in Industry.
- March 20, Adequate Nutrition for the Industrial Worker.
- March 27, Medical and Health Services in Industry.
- April 3, Preventive Industrial Medicine.
- April 10, Legal Aspects of Occupational Diseases.

Dr. Louis H. Nahum, New Haven, is chairman of the program committee of the Clinical Congress of the state medical society.

DELAWARE

Society News.—Dr. George E. Bennett, Baltimore, discussed problems of knee joint surgery before the New Castle County Medical Society, November 19, in Wilmington.—A symposium on glaucoma is being presented by the section of ophthalmology and otolaryngology of the Delaware Academy of Medicine, Wilmington, in three meetings, November 19, December 17 and January 21. Included among the speakers are Drs. William O. LaMotte, Richard R. Tybout, Gerald O. Poole, Norman L. Cutler and William R. Hazzard.

DISTRICT OF COLUMBIA

Personal.—Dr. Rex E. Buxton, Boston, has been appointed director of the Washington Institute of Mental Hygiene, succeeding Dr. Paul J. Ewerhardt, resigned.—Dr. James A. Gannon has been appointed a member of the District board of education, newspapers report.

Society News.—Dr. Jesse G. M. Bullowa, New York, addressed a meeting of the medical and dental officers of the navy on duty in the District and vicinity, November 4, on "The Appropriate Therapy of the Pneumonias."—Dr. Everts A. Graham, St. Louis, addressed the monthly meeting of Army Medical Department officers in Washington and vicinity at the Army Medical Center, November 18, on "Surgery of the Chest." Dr. Henry K. Mohler, Philadelphia, spoke, October 14, on "Use of Sulfanilamide and Its Associated Compounds."

GEORGIA

Industrial Hygiene Service.—The Georgia Department of Public Health has established an industrial hygiene service as a part of the division of preventable diseases to meet the increasing needs of advisory service to industries in the protection and promotion of the health of industrial workers. The service, consisting of medical and engineering advisory assistance, will soon be available to all types of industries.

Pediatric Meeting.—The Georgia Pediatric Society met at the Biltmore Hotel, Atlanta, December 12. The speakers included:

- Dr. Lee Edward Farr, Wilmington, Del., Prognostic Value of Renal Function Tests in Nephritis: Role of Diet in the Therapy of Nephritis.
- Dr. Samuel Z. Levine, New York, The Handicaps of Prematurity and How to Meet Them: Water and the Growing Organism.
- Dr. Edward F. Bland, Boston, Manifestations of Rheumatic Fever in Childhood: Course of Rheumatic Heart Disease in Childhood and Adolescence.

Personal.—Dr. Joseph A. Johnson, Greensboro, resigned as head of the Greene County health unit, effective November 1, to accept a similar position at Toccoa in charge of the unit including Stephens, Habersham and Rabun counties.—Dr. James A. Thrash, health officer of Columbus and of Muscogee County, has been granted leave of absence until June 1941 to take special studies in health work at the University of North Carolina School of Medicine, Chapel Hill.—Dr. Roy L. Johnson, Douglas, has resigned as health commissioner in Coffee County to enter private practice.—Dr. Robert V. Schultz, New York, has been named director of public health education for the state department of health.

ILLINOIS

Society News.—Dr. Adolph L. Sahs, Iowa City, discussed "The Common Neuroses" before the Adams County Medical Society, November 11.—A symposium on diseases of the biliary tract was presented before the Coles-Cumberland County Medical Society in Mattoon, November 7, by Drs. Karl A. Meyer and Manuel E. Lichtenstein, Chicago.—Dr. Oscar F. Schultz, Evanston, was elected president of the Illinois Society of Pathologists at its annual meeting, December 7; Dr. Israel Davidsohn, Chicago, is the secretary.

Chicago

Society News.—Dr. George J. Garceau, Indianapolis, addressed the Chicago Orthopedic Society, December 13, on "Treatment of Scoliosis" and Dr. Fremont A. Chandler, "Aseptic Necrosis of the Head of the Femur."—The Chicago Pediatric Society was addressed, December 17, by Dr. Alvin C. Rambar, among others, on "The Opsono-Cytophagic Test in Pertussis Inoculation."

Study Group Named in Honor of Dr. Sonnenschein.—A medical history study group has been organized at the Michael Reese Hospital and named in honor of the late Dr. Robert Sonnenschein. The first meeting of the new group, December 11, was addressed by Dr. Reuben Friedman, assistant professor of dermatology and syphilology, Temple University School of Medicine, Philadelphia, whose subject was "Acarus Scabiei—The Story of a Twelve-Hundred Years' Search for the Obvious."

Mr. Bacon Retires as Superintendent of Presbyterian Hospital.—After more than forty years' service at Presbyterian Hospital, Asa S. Bacon will retire as superintendent, January 1. He will be succeeded by J. Dewey Lutes, who has been superintendent of Ravenswood Hospital for the last nine and one-half years. Mr. Bacon is a trustee of the American Hospital Association and has been its treasurer for thirty-five years, with the exception of one year when he served as president. In recognition of his long service, the association last February named its reference library at 18 East Division Street the Asa S. Bacon Library.

INDIANA

Personal.—Dr. George R. Douglas, Valparaiso, has been appointed health officer of Porter County, filling the vacancy caused by the death of Dr. Herman O. Seipel.

District Meeting.—Dr. Harry A. Towsley, Ann Arbor, Mich., recently addressed the Seventh District Medical Society in Franklin on "Diagnosis and Treatment of Acute Contagious Diseases." He also showed a colored motion picture on the acute stages of exanthemas.

Society News.—A symposium on arthritis was conducted before the Madison County Medical Society, November 18, in Anderson by Drs. Francis M. Williams, Frederick B. Wishard, Aubrey W. Elsten and Paul T. Lamey. All are from Anderson. —Dr. Norman E. Freeman, Philadelphia, discussed "Peripheral Circulatory Failure: Its Prevention and Treatment" before the Indianapolis Medical Society November 26. —Dr. Thomas M. Conley, Kokomo, discussed "Brain Tumors in Children" before the Howard County Medical Society in Kokomo, November 1.

LOUISIANA

Carville Patients Honor Perry Burgess.—The Patients' Federation and the American Legion Post of Carville, comprised entirely of leper patients, gave a reception in honor of Mr. Perry Burgess, president of the Leonard Wood Memorial, New York, and author of the book "Who Walk Alone," at the Marine Hospital, Carville, November 27. The welcome to Mr. Burgess was for the work he has been doing in behalf of leper patients. "Who Walk Alone" is the story of an American soldier who served in the Spanish-American War in the Philippines, and who became a leper many years after he had returned home.

MAINE

Society News.—Dr. Eugene E. O'Donnell discussed problems of intestinal surgery before the Portland Medical Club recently. —The York County Medical Association was addressed in Biddeford, October 9, by Dr. William J. Brickley, Boston, medical examiner for Suffolk County, on "Cause and Manner of the *Squalus* Deaths."

MARYLAND

Regulations for Occupational Diseases.—At a meeting, October 14, the Maryland State Board of Health adopted regulations for the control and prevention of occupational diseases, effective January 1. The Baltimore City Department of Health and the division of industrial hygiene of the United States Public Health Service cooperated in the formulation of the regulations. Regulation 1 is as follows:

No persons, firm, corporation or other employer shall use or permit to be used in the conduct of his business, manufacturing establishment or other place of employment, any process, material or method of working known to have an adverse effect on health, unless arrangements have been made to maintain the occupational environment in such a manner that injury to health shall not result.

Regulation 2 pertains to concentration limits and reads:

Exposures to dusts, fumes, mists, vapors, gases, or any materials that may affect health shall be kept below the following concentration limits:

Material	Concentration
Benzene (Benzol)	75 parts per million
Carbon tetrachloride	100 parts per million
Carbon monoxide	100 parts per million
Chlorine	1 part per million
Chromic acid	0.1 mg. per cubic meter

MASSACHUSETTS

Society News.—The New England Pathological Society was addressed, November 21, by Dr. Harry S. N. Greene, Princeton, N. J., on "Development of Autonomy in Spontaneous Rabbit Tumors." —Dr. Otto J. Hermann, Boston, discussed "Convalescent Care of Fractures" before the New England Society of Physical Medicine, November 21, in Boston. —The Essex South District Medical Society was addressed, December 4, by Dr. Walter Bauer, Boston, on "Diagnosis and Treatment of the Commoner Arthritides." Dr. James C. White, Boston, will address the society in Hathorne, January 8, on "Visceral Pain and Its Relief." —Dr. Thomas M. Rivers, New York, delivered a Robert Dawson Evans Memorial Lecture in the Evans Memorial Auditorium, Massachusetts Memorial Hospitals, Boston, November 19, on "Elementary Bodies of Vaccine."

MICHIGAN

Changes in Health Officers.—Dr. Lorin E. Kerr, Toledo, has been appointed director of the Iron County health department, succeeding Dr. Thomas E. Camper, who is on leave of absence for graduate study at the University of Michigan, it is reported. —Dr. Buell H. Van Leuven, Petoskey, has been named health officer of Menominee County to succeed Dr.

Clifford C. Corkill, who is studying at the Johns Hopkins University School of Hygiene and Public Health, Baltimore.

Society News.—Dr. Robert E. Lee, Chicago, discussed "Ambulatory Treatment of Varicosities and Associated Pathology" before the Muskegon County Medical Society, November 15. —Dr. Winthrop Morgan Phelps, Baltimore, addressed the Calhoun County Medical Society, November 18, on "The Spastic Child" and Dr. Robert B. Malcolm, Chicago, November 12, "Surgical-Pathological Conditions of the Neck." —Dr. Richard H. Freyberg, Ann Arbor, addressed the Washtenaw County Medical Society, Ann Arbor, November 12, on "Treatment of Chronic Arthritis." —The medical section of the Wayne County Medical Society was addressed, November 11, by Dr. Joseph T. Wearn, Cleveland, on "Changes in the Coronary Circulation Resulting from Normal and Abnormal Processes." —Among others, Dr. Frederick F. Yonkman, Detroit, addressed the Detroit Physiological Society, November 14, on "Depression of the Sympathetic Nervous System."

Annual Clinic of Highland Park Physicians' Club.—The fifteenth annual clinic of the Highland Park Physicians' Club was conducted at the Highland Park General Hospital, November 6. Included among the speakers were:

Dr. Andrew C. Ivy, Chicago, Medical Treatment of Gallbladder Disease.
Dr. Plinn F. Morse, Detroit, Pathology of Gallbladder Disease and Its Effect on the Human Body.
Dr. Willis D. Gatch, Indianapolis, Surgical Treatment of Gallbladder Disease.
Dr. Frederick A. Collier, Ann Arbor, Shock: Differential Diagnosis and Treatment.
Mr. P. A. Pranion, Detroit, Demonstration of Falling Drop Method.
Dr. Marion A. Blankenhorn, Cincinnati, Recent Advances in Vitamin Therapy.
Dr. Russell L. Haden, Cleveland, Rheumatoid Arthritis—Etiology and Treatment.
Dr. David S. Hillis, Chicago, Diagnosis of Disproportion Between Head and Pelvis.

MINNESOTA

The Bell Lecture.—Dr. Leroy U. Gardner, director, Saranac Laboratory for the Study of Tuberculosis, Saranac Lake, N. Y., delivered the seventh annual John W. Bell Lecture before the Hennepin County Medical Society, Minneapolis, December 2. His subject was "Manifestations of Tuberculosis in the Silicotic Patient."

MISSOURI

Personal.—Members of the executive faculty and the library staff of Washington University School of Medicine, St. Louis, recently observed the twenty-fifth anniversary of Miss Ella B. Lawrence as librarian. A silver bowl was presented to Miss Lawrence. —Dr. Lawrence T. Post, who recently retired as editor of the *American Journal of Ophthalmology*, was guest of honor at a dinner given by the St. Louis Ophthalmic Society at the University Club, St. Louis, November 27.

Society News.—A symposium on pneumonia was conducted before the Jackson County Medical Society, Kansas City, November 26, by Drs. John Aull, Harvey P. Boughnau and Lindsay S. Milne. All are of Kansas City. —Dr. Milton C. Winternitz, New Haven, Conn., addressed the Kansas City Academy of Medicine, November 15, on "Experimental Studies on Arteriosclerosis." —The Kansas City Society of Obstetrics and Gynecology was addressed, November 7, by Clarence W. Sondern, Ph.D., on "Newer Information on Estrogenic Substances." —Dr. Robert M. Isenberger addressed the Kansas City Urological Society, November 7, on "Pharmacology of the Urinary Antiseptics." —A symposium on infantile paralysis was presented before the Buchanan County Medical Society, St. Joseph, November 6; the speakers were Drs. William J. Hunt, Walter Roger Moore and Jacob Kulowski. All are from St. Joseph.

MONTANA

Personal.—Dr. John H. Garberson, Miles City, was recently elected governor of district 112 of the Rotary International.

Another Medical Supplement.—An eight page Health Section was published on October 13 by the *Sunday Democrat-News*, Lewiston, in cooperation with the Fergus County Medical Society.

NEBRASKA

Society News.—Dr. Newell C. Gilbert, Chicago, addressed the Omaha-Douglas County Medical Society, Omaha, November 12, on "Reflex Variations in Coronary Blood Flow." Dr. Claude F. Dixon, Rochester, Minn., was the speaker December 10 on "Surgical Diseases of the Colon." —The Five County and Madison Six County medical societies held a joint meeting in Norfolk, November 19. A symposium on fractures was presented by Drs. Robert D. Schrock and James W. Martin, Omaha, and George A. Haslam, Fremont.

NEW YORK

Institute on Radiology at Syracuse.—An institute on radiology will be held at the Syracuse University College of Medicine, Syracuse, January 18, under the sponsorship of the Central New York Roentgen Ray Society, the Medical Society of the State of New York, the division of cancer control of the New York State Department of Health and the medical college. Speakers in the afternoon will be:

Edith H. Quimby, associate physicist, Memorial Hospital, New York, Physics of Radiation for the Radiologist.

Dr. Merrill C. Sosman, Boston, Roentgenologic Aspects of Brain Tumors, Diagnosis and Treatment.

Dr. Ursus V. Portmann, Cleveland, Indications and Results of Roentgen Therapy.

Dr. Fred W. Stewart, New York, Radiosensitivity of Tumors.

Dr. Stafford L. Warren, Rochester, The Cyclotron.

At a dinner meeting Dr. Roscoe R. Spencer, assistant chief of the National Cancer Institute, U. S. Public Health Service, Bethesda, Md., will be the speaker.

New York City

Lecture on Digitalis.—Dr. Harry Gold, assistant professor of pharmacology, Cornell University Medical College, will deliver a lecture at New York Medical College, January 17, under the auspices of the Omicron chapter of Phi Delta Epsilon. Dr. Gold's subject will be "Some Recent Studies on Digitalis."

Photographic Contest for Social Hygiene Program.—The Society for the Study of Syphilis, in cooperation with the Metropolitan Camera Club Council and the U. S. Public Health Service, is sponsoring a competition for photographs to be used in public health education in venereal disease control. Merchandise prizes will be awarded for the ten best entries. For rules, the society may be addressed at Room 329, 125 Worth Street.

Personal.—Dr. Jack Masur, assistant director of Montefiore Hospital, has been appointed director of Lebanon Hospital. He will assume the position January 1, succeeding Mr. George E. Halpern, who is retiring after twenty-three years of service. Dr. Edwin L. Demuth will succeed Dr. Masur at Montefiore Hospital.—Dr. Charles F. W. Bove, for many years on the staff of the American Hospital of Paris, recently joined the staff of Gotham Hospital. Dr. Bove, a native of New York, went to France during World War I.

Dr. Humpstone Honored.—Dr. O. Paul Humpstone, chief of the department of obstetrics and gynecology at the Methodist Hospital, Brooklyn, was honored at a dinner marking his retirement from that position, December 6. Dr. Humpstone, a graduate of Columbia University College of Physicians and Surgeons in 1899, served his internship at the Methodist Hospital and has been associated with the hospital ever since. He is also professor of clinical obstetrics and gynecology at Long Island College of Medicine. At the dinner Bishop Francis J. McConnell of the Methodist Church paid tribute to Dr. Humpstone and Ralph Emerson Davis, pastor of St. Mark's Methodist Church and a member of the hospital's board of managers, presented to the guest of honor a leather-bound testimonial which bestowed on him the title of director emeritus of the division of obstetrics and gynecology.

NORTH CAROLINA

Portrait of Dr. Manning.—The alumni association of the University of North Carolina School of Medicine, Chapel Hill, recently presented to the university a portrait of Dr. Isaac H. Manning, Kenan professor emeritus of physiology and former dean of the school. Dr. William Raney Stanford, Durham, a former student under Dr. Manning, made the presentation and President Frank P. Graham accepted for the university.

Society News.—Dr. William S. Justice, Asheville, discussed "Use and Abuse of Vitamin K" before the Buncombe County Medical Society, Asheville, November 18.—Dr. James E. Bullitt, Chapel Hill, was elected president of the North Carolina Pathological Society at its annual meeting in Charlotte, November 19, and Dr. Coy C. Carpenter, Wake Forest, reelected secretary. Dr. Charles F. Geschickter, Baltimore, was the guest speaker on "Benign and Malignant Breast Tumors."

OHIO

Morris Memorial Lecture.—The fifth annual Roger S. Morris Memorial Lecture was presented at the University of Cincinnati College of Medicine, December 11, by Bradley M. Patten, Ph.D., professor of anatomy, University of Michigan Medical School, Ann Arbor. His subject was "Age Changes

in Embryonic Heart Action as Recorded in Micro-Moving Pictures and Studied Electrocardiographically."

Physicians Elected to Legislative Bodies.—Dr. Frederick C. Smith, Marion, was reelected to Congress from the eighth Ohio district, the *Ohio State Medical Journal* reports. Drs. Henry T. Phillips, Athens, and Everett LeFever, Glouster, were reelected to the state general assembly and Drs. George G. Hunter and Forrest R. Stewart, Ironton, were elected to the state senate and house of representatives, respectively.

Veteran Physicians Honored.—Dr. Norval A. Hamilton, Franklin, was guest of honor recently at a testimonial dinner attended by physicians and other friends of the Miami Valley area to celebrate his completion of fifty years in practice. Dr. Martin H. Fischer, Cincinnati, made the principal address. Dr. Hamilton was presented with a watch.—Gold plaques were presented to three physicians who have practiced fifty years or more by the Highland County Medical Society at a meeting in Hillsboro, November 6. They were Drs. John A. Mercer, Greenfield; Thomas W. Roberds, Belfast, and J. Barrett Kleckner, Lynchburg.—Six Medina County physicians who have practiced twenty-five or more years in the county were honor guests at a meeting of the Medina County Medical Society in Medina, November 14. They were Drs. Hiram P. H. Robinson, Medina; Harry Streett and Walter H. Scudder, Litchfield; Ernest L. Crum, Lodi; Edwin J. Kooztz and Robert L. Johnson, Wadsworth.

OREGON

Meeting of Specialists.—The North Pacific Society of Neurology and Psychiatry held a meeting at the University of Oregon Medical School, Portland, November 9. The morning program included the following speakers: Drs. John L. Haskins, Portland, "Statistics on Admissions, Cost and Attendant Ratio of Private and State Mental Hospitals in the Northwest"; De Witt C. Burkes, Portland, "Familial Cerebellar Degeneration," and Robert H. Southcombe, Spokane, Wash., "Pyknolepsy." In the afternoon a neurologic symposium was presented as follows: Drs. John E. Raaf, Portland, "Lindau's Disease"; Charles O. Sturdevant and Thomas D. Robertson, Portland, "Multiple Sclerosis"; Laurence Selling, Portland, "Syringomyelia," and Charles P. Larson, Tacoma, Wash., and Vinton D. Sneed, Portland, "Amaurotic Familial Idiocy (Tay-Sachs Disease)." George Bernard Noble, Ph.D., professor of political science, Reed College, Portland, was the dinner speaker.

PENNSYLVANIA

Society News.—Drs. John Royal Moore and William Edward Chamberlain, Philadelphia, addressed the Locomotion County Medical Society, Williamsport, December 13, on "Delayed Reduction of Fractures," discussing surgical and clinical aspects and roentgenologic aspects, respectively.—Dr. Richard J. Behan, Pittsburgh, addressed the Fayette County Medical Society, Uniontown, December 5, on "Diagnosis and Control of Cancer."—Dr. Percy S. Pelouze, Philadelphia, addressed the Delaware County Medical Society, Chester, December 12, on "Urinary Bladder in Health and Disease."—Dr. Stephen A. Forbes, State College, addressed the Centre County Medical Society, Bellefonte, December 12, on "Backache, Its Causes and Treatment."—Dr. Murray B. Ferderber, Pittsburgh, discussed "The Selection of Heat in Physical Medicine" before the Mercer County Medical Society, Farrell, December 11.—Dr. William H. Guy, Pittsburgh, addressed the Blair County Medical Society at Altoona in November on "Dermatologic Manifestations of Syphilis."

Philadelphia

Annual Gross Lecture.—Dr. Virgil H. Moon, professor of pathology, Jefferson Medical College, delivered the annual Gross Lecture of the Pathological Society of Philadelphia, December 12, on "Pathology and Vascular Dynamics of Shock."

Society News.—At a meeting of the Eastern Pennsylvania Chapter of the Society of American Bacteriologists, November 26, the speakers were Dr. Esmond R. Long and Agnes B. Vogt on "Relation of Sex to the Course of Experimental Tuberculosis in Mice"; Dr. Max B. Lurie, "Relationship of Hereditary Constitution and Immunologic Factors in Resistance to Tuberculosis"; Florence B. Seibert, Ph.D., and Mr. John T. Glenn, Glenolden, Pa., "Improvements in the Preparation of Purified Protein Derivative Tuberculin," and Dr. Joseph D. Aronson, with Dr. Robert M. Saylor and Erna I. Parr, U. S. Indian Medical Service, "Incidence of Coccidioides Immitis Infection in Some Parts of the United States."

SOUTH DAKOTA

Personal.—Dr. Alpha J. Campbell, recently of Los Angeles, has been appointed chief medical officer at the Veterans' Administration Facility, Hot Springs.

Public Health Meeting.—The annual meeting of the South Dakota Public Health Association was held in Huron, October 28, with Dr. Gaylord W. Anderson, Minneapolis, as the guest speaker. Dr. Anderson spoke on "Tuberculosis Control Through Epidemiologic Investigation" and "Role of the Part-Time Health Officer."

TENNESSEE

Regional Meeting.—The semiannual meeting of the Middle Tennessee Medical Association was held in Franklin, November 21. Among other speakers were Drs. Frank J. Runyon, Clarksville, on "The Therapy of Malaria, Especially Stressing an Improved Therapeutic Test"; Tinsley R. Harrison, Nashville, "Some Clinical Aspects of Pain in the Chest"; Roscoe C. Gaw, Gainesboro, "Upper Respiratory Tract Infections and Their Influence on the Pulmonary System," and Granderson Hearn Bradley, Nashville, "Vitamins B and K in Pediatrics."

Dr. Blalock Honored for Research.—Dr. Alfred Blalock, professor of surgery, Vanderbilt University School of Medicine, Nashville, received the research medal of the Southern Medical Association at the annual meeting in Louisville, Ky., in November. The award was made in recognition of Dr. Blalock's research on circulation of the blood in cases of shock. Dr. Blalock graduated from Johns Hopkins University School of Medicine, Baltimore, in 1922 and went to Vanderbilt for a residency in 1925, becoming assistant professor of surgery in 1927 and professor in 1937.

WISCONSIN

The Bardeen Lecture.—Dr. Ernest E. Irons, Chicago, delivered the annual Charles R. Bardeen Memorial Lecture at the University of Wisconsin Medical School, Madison, December 6, on "Aspiration Pneumonia: Pathology-Bacteriology-Symptoms." The lecture is sponsored by the Phi Chi fraternity.

In Memory of Dr. Dearholt.—An all day meeting in memory of the late Dr. Hoyt E. Dearholt, Milwaukee, for many years executive secretary of the Wisconsin Anti-Tuberculosis Association, was held at the University of Wisconsin Medical School, Madison, November 26, under the auspices of the tuberculosis association and the university. Dr. James Burns Amberson Jr., New York, the guest speaker, discussed "Diagnosis of Pulmonary Tuberculosis" and "Principles of Treatment of Tuberculosis."

Society News.—Dr. Tracy J. Putnam, New York, addressed the University of Wisconsin Medical Society, Madison, November 22, on "Physiology and Treatment of Paralysis Agitans and Athetosis."—Drs. Malcolm G. Gillespie and Edward L. Tuohy, Duluth, Minn., addressed a recent meeting of the Polk County Medical Society, Webster, on "Vitamin K in Cases of Liver Depletion With and Without Jaundice" and gout.—Drs. Robert B. Osgood, Boston, and Albert A. Mertz, Decatur, Ill., addressed the Milwaukee Society of Clinical Surgery, November 26, on "Backgrounds of Bone and Joint Surgery" and "Advance in Treatment of Fractures of the Hip" respectively.—Dr. Everett D. Plass, Iowa City, addressed the Medical Society of Milwaukee County, Milwaukee, November 8, on "Newer Advances in the General Field of Obstetrics."

GENERAL

The Bombing of England's Hospitals.—Despite the German claim that their bombing is confined to military objectives, the fact is, the Manchester *Guardian Weekly* says, that numerous nonmilitary objectives, including hospitals, churches, world famous buildings, stores, clubs, newspaper offices and other nonmilitary objectives have been bombed. The following are some of the hospitals that have been hit:

London Hospital	Swiss Relief Center
Queen Mary's Hospital	Great Ormond Street Hospital
St. Bath's Medical School	St. Dunstan's Hospital
St. Thomas's Hospital	Tunbridge Wells Hospital
Chatter House Clinic	Royal Hospital (Chelsea)
Ford's Hospital	Royal College of Surgeons
Coventry Hospital	

Honored for Aid to China.—Medals of honor for distinguished service to China were presented, October 25, to eleven members of the board of directors of the American Bureau for Medical Aid to China by Dr. Fu-Ching Yen, formerly national health administrator of China. Those so honored included Drs. James B. Murphy, Farn B. Chu and George B. Wallace, New York; Homer W. Smith, S.C., professor of

physiology, New York University; Dr. George Morris Piersol, Philadelphia, and Dr. Robert R. Hannon, Albany, N. Y. Certificates accompanying the medals bore the signature of Chiang Kai-Shek and the official seal of the Executive Yuan and paid tribute to the work of the recipients for relief of China's war sufferers.

Census of Medical Manufactures.—The U. S. Bureau of the Census has released additional figures showing in detail the production of surgical supplies and equipment, orthopedic appliances and kindred products and a separate report on rubber products for use in hospitals and by the medical profession. An earlier report appeared in *THE JOURNAL*, November 23, page 1817. The figures are for the year 1939.

Manufacturing establishments devoted mainly to the production of surgical supplies and equipment, orthopedic appliances and kindred products produced goods during 1939 valued at the factory at 3 per cent more than those produced during 1937.

During 1939 the 360 establishments operating in this industry turned out merchandise estimated by the producers at \$79,398,442. In 1937 the 323 establishments then included valued the output for that year at \$77,068,094.

The 360 factories also spent nearly \$5,000,000 less for materials, supplies, fuel, purchased electric energy and contract work in 1939 than did the 323 establishments two years before: \$40,296,584 in 1939 compared with \$45,030,602 in 1937, a difference of 10.5 per cent. With production up and cost down, the value added by manufacture was 22.1 per cent higher in 1939 than in 1937. The value added by manufacture is the value of products after the cost of materials, supplies, fuel and the like has been subtracted. This total amounted to \$39,101,858 last year, compared with \$32,037,492 in 1937.

Of the \$79,398,442 worth of products manufactured by the 360 factories last year, \$66,108,877 represented the value of surgical supplies and equipment not elsewhere classified, and orthopedic appliances alone. The difference between the first and the last quoted figure includes \$223,582 received for contract work and \$13,065,983 worth of products classified in other industries. In all instances the 1939 total was higher than that for 1937, when a breakdown of the production of the 323 plants in the industry revealed that \$65,328,236 represented the value of surgical supplies and equipment and orthopedic appliances made, \$158,444 the value of contract work and \$11,581,414 the value of secondary products.

An incomplete report on the value of surgical supplies and equipment and orthopedic appliances produced in other industries last year puts the figure at \$5,571,103. In 1937 this figure, when finally computed, was \$5,788,762. Complete figures on this item will not be available until the final report for 1939 is issued.

The factory value of crutches, fracture appliances, elastic hosiery, abdominal supporters, braces, arch supporters, absorbent cotton and medicated plasters made during 1939 was higher than the value of those produced in 1937, while the output of artificial limbs, stumpsocks, surgical belts, suspensories, trusses, surgical gut strings, nonmedicated adhesive plasters, bandages and surgical gauze and dressings had a higher factory value in 1937 than last year.

Though the 1939 figures on sanitary napkins were not all in at the time the preliminary report was sent to the printer, the incomplete figures disclose that it was the biggest single item turned out by the industry last year. The value of the sanitary napkins so far reported is \$12,984,464. In 1937 factories reported the production of this item at \$14,418,756. That year, too, it was the major item turned out by the industry.

For the first time hospital, surgical and other sterilizers have been reported separately. Last year's output of these goods was valued at \$1,153,680 by the manufacturers' estimates.

All figures in the report are preliminary and in several cases incomplete. These figures are subject to revision before being published in final form. Plants that had a production of less than \$5,000 last year are not included in Census of Manufactures reports.

Rubber products having a value at the factory of at least three million dollars were manufactured last year. Production of hospital sheeting was valued at \$1,639,519, a substantial gain over the 1937 figure of \$1,072,522. These prices cover quantities of 3,857,247 square yards in 1939, compared with 2,982,123 square yards in 1937.

Surgeons' gloves produced last year had a value of \$1,099,605, numbering 851,581 dozen pairs. No separate figures were obtained for this category in 1937.

In addition, an undetermined amount of medical and surgical hard rubber products are included in the 1939 total of \$7,037,325 for medical and druggists' rubber sundries other than water bottles, fountain syringes, nipples and pacifiers.

Foreign Letters

BUENOS AIRES

(From Our Regular Correspondent)

Oct. 24, 1940.

Fifth Pan American Congress for Tuberculosis

The fifth Pan American Congress for Tuberculosis, in which eleven Spanish American countries with 150 delegates participated, was held in Buenos Aires and Córdoba, October 13-17. The United States was represented by Dr. Henry C. Sweany. The Oficina Sanitaria Panamericana in Washington was represented by Dr. Henson as observer. The congress was held under the auspices of the Latin-American Union of Societies for Tuberculosis, in which Argentina, Bolivia, Brazil, Colombia, Chile, Cuba, Mexico, Paraguay, Peru, Uruguay and Venezuela hold membership. Dr. Gumersindo Sayago, professor in Córdoba, presided. Argentina was represented at the opening meeting by Dr. R. S. Castillo, acting president of the Argentine Republic. The sessions were formally opened by Dr. G. Rothe, minister of the Department of Justice and Public Instruction. Dr. G. Sayago, president of the congress, linked his remarks in his opening speech to one of the chief subjects of discussion, the indexes of tuberculization in South America. He pointed out that the reports submitted by the individual countries, members of the congress, clearly revealed the presence of a common epidemiologic problem, in that tuberculosis had spread to a great extent in a uniform way. Similar geographic, racial, economic and social problems prevailed. The environmental factors of tuberculosis in Spanish American countries differed greatly from those of other countries with an older civilization. In these, general sanitation was more advanced and tuberculization had had a wider sweep. South American countries, on the other hand, rather resembled countries in which tuberculosis appeared as a new disease. Only the large South American cities presented an epidemiology analogous to that of other countries. In spite of the declining mortality rate, tuberculosis still constituted a social problem of the greatest significance. Beds available for tuberculous patients in South America were insufficient and increased the hazards of infection in the homes. Even where conditions were most favorable there was only one bed for from three to four patients who died of the disease. No effective tuberculosis control was possible without the isolation of infected persons.

The first deliberative session was held on the second day with the "Indexes of Tuberculization in South America" as the leading subject. Alejandro A. Raimondi and Julio Palacio, members of the Argentine delegation, defined the term index as representing the percentage of persons of a certain age, collectivity, race or religion who had been tubercularized. The average index for Argentina was as follows: from 0 to 6 years 44.5 per cent, from 7 to 14 years 54.1 per cent, from 15 to 20 years 67.3 per cent and above 20 years 72.3 per cent. Female incidence preponderated until the fourteenth year. The examination of 84,854 males and females at all age levels showed that 64.8 per cent presented sensitivity. Primary infection, formerly contracted more often in childhood, now appeared more often in early adulthood, the index fluctuating in Argentina between 26 and 84.2 per cent (the latter for Buenos Aires). The index for children of school age in Buenos Aires varied from 75.53 per cent in central locations to 32 in one of the suburbs. Everywhere the incidence was much lower in rural districts. Epidemiologically, tuberculous infections in Argentina show different stages of evolution regionally. In Jujuy, in the northern part of the state, a high index of 71.9 per cent prevailed together with a high mortality rate of 23.9 per 10,000 inhabitants. In the large cities, while the index was high, the mortality rate was on the decline.

In Bolivia, the epidemiologic index for the cities is high and is related to their economic condition. Because of the great frequency of anergy, vaccination with BCG is extensively recommended. In Brazil, owing to limited funds, the index remains high in comparison with European countries, which showed a decline during the last fifteen years at the ages below 20 years. Surveys in Brazil are not complete. Chile is still in the stage of massive tuberculization. The percentage of the allergic at the age of 6 years is high and the index at age 15 is 80 per cent. In Cuba the infection index, based on about 54,000 persons examined in Havana, was as high as 74 per cent in persons regarded as normal, and the morbidity rate 4 per cent; whereas it amounted to 11.7 per cent in sections of the population in which there was contact with the tuberculous. In Peru, children between 1 month and 16 years of age living in an infected environment and with tuberculin-positive reactions gave an index of 56.9 per cent, whereas in Lima, the capital of Peru, the index for children between 6 and 16 years in an apparently normal environment amounted to 65.3 per cent. In Uruguay great interest was exhibited in creating careful case lists and in the usual tuberculin tests. Sensitivity to the Mantoux test in relation to Pirquet's test was as follows: From the sixth year on the Mantoux test added 20 per cent of allergic cases to those discovered by the Pirquet tests if the positive results of the Pirquet test did not exceed 75 per cent. The formulation of international classification standards was recommended for the purpose of describing roentgenologic observations. At present great difficulties exist for the evaluation of allergy. It was also recommended that the next Pan American Congress for Tuberculosis request its member countries to conduct a systematic examination of the whole population. This would undoubtedly lower the index. In Venezuela, tuberculosis represents one of the most serious problems of public health. The mortality rate in the cities from tuberculosis varies from 210 to 470, with an average of 321 per hundred thousand inhabitants. In certain cities the mortality ranges from 12.3 to 23.16 per cent. An active pulmonary infection rate of 1.52 per cent was found in children of school age and a 3.58 per cent rate in pregnant women. The morbidity incidence is high, especially in the first years of life. It recedes between the tenth and the nineteenth year but rises again and attains its peak at age 30. No noteworthy differences in this respect were found between white and Negro persons.

HEREDITY

The subject for the second day was Heredity and Infection. Dr. A. Cetrángolo, representing the Argentine delegation, pointed out that, since immunity was not hereditary, it was difficult to understand how heredity could possess any decisive influence in evolving a human type capable of greater resistance to tuberculosis. The tuberculosis-resistant type does not represent the transmission of specific immunity but is a selective phenomenon. If the factor of heredity were as significant as assumed, the population of Europe, which had been in contact with tuberculosis for so many centuries, would be completely immune by this time. Moreover, the mortality rate for tuberculosis would not mount with economic crises. In infections, intensive bacillary invasion in persons with low nonspecific resistance evokes great hypersensitivity and low relative immunity and induces caseous processes; on the other hand, infections with low bacillary concentration provoke processes of a weakened hypersensitivity but with high relative immunity resulting in mitigated processes and allergy without morbidity. A connection exists between heredity and infection. Both factors cooperate with other factors and either promote or repel bacillary invasion. During the evolution of an infection, either grave or mild conditions will prevail in accordance with the concentration of bacilli. Heredity has only genotypic significance and is unable to bestow a specifically greater resistance.

The sessions of the third day of the congress were held in the city of Córdoba. The faculty of medicine of Córdoba has clinical opportunities because of the many sanatoriums situated in the clinically suitable province of the same name. Dr. Sofanor Novillo Corvalán, rector of the University of Córdoba, pointed out that since the first Pan American Congress held in Córdoba in 1927 the mortality incidence for tuberculosis in the city had decreased from 28.1 per 10,000 inhabitants to 17.9 in 1935, representing a reduction of 40 per cent, attributed to the systematic control of the disease. In behalf of the committee of organization, Raimondi stressed the necessity of cooperation of all South American countries. Several of these countries had recently showed an increase of tuberculosis and thus presented new problems to be solved. Population sections, immune until then, needed to be vaccinated with BCG. The European war constitutes a cause of anxiety also for the peoples of South America, because in the years to come the same factors would make themselves felt, such as a social imbalance, impoverishment and economic difficulties of all kinds. These factors either singly or collectively could lead to the spread of tuberculosis.

EXTRAPULMONARY TUBERCULOSIS

The paper, presented by Dr. Raúl A. Vaccarezza and José B. Gómez, was based on clinical and roentgenologic examinations of 420 male and female patients with extrapulmonary tuberculosis varying in age and degree of infection. Lung modifications were found in 90.2 per cent, a detailed analysis of which was presented to the congress. Extrapulmonary tuberculosis, they concluded, does not generally behave like isolated chronic tuberculosis of other body organs but tends, simultaneously or concomitantly, to become established in the systems of other organs, including the lung. Extrapulmonary tuberculosis and pulmonary tuberculosis are not mutually exclusive or antagonistic. On the contrary, the two increasingly combine. If the etiology of a disease is obscure and at the same time hematogenic modifications of the lung are observed, tuberculosis should be suspected. Patients with extrapulmonary tuberculosis ought not to be consigned to general hospital wards but be given special wards. So-called isolated chronic tuberculosis affecting an organ is not to be regarded as a local lesion but as a general condition capable of infecting other organs.

The Brazilian delegates were of the opinion that extrapulmonary cases generally represented metastasis of pulmonary lesions which spread by way of the blood stream. The Chilean delegates were in accord with this point of view and pointed out that 61 per cent of all cases of extrapulmonary tuberculosis were associated with active pulmonary lesions, 59 per cent of which represented reinfections and 2 per cent primary infections. In from 50 to 55 per cent the pulmonary pictures accompanying extrapulmonary tuberculosis show advanced and extensive lesions. Among them the mixed type predominates (31 per cent), with the diffused miliary type next in frequency (16 per cent). The presence, type and evolution of pulmonary lesions determine the prognosis of the extrapulmonary forms. Surgical wards should be established in hospitals for tuberculous diseases, closely cooperating with specialists in the field of tuberculosis. The age level at which extrapulmonary tuberculosis appears and its evolution create problems of invalidism and social dependence that make such centers desirable. Paraguay's delegates presented an extensive statistical tabulation of extrapulmonary tuberculosis occurring in their country. Peru's delegates called attention to the fact that extrapulmonary tuberculosis had not received sufficient attention in the fight on tuberculosis. Pure extrapulmonary forms, free from active pulmonary infections, amount to 24 per cent. Isolated extrapulmonary tuberculosis has mostly a renal or osteo-articular site. If pulmonary infections and extrapulmonary lesions coexist, the latter are generally of a secondary nature, indicating the collapse of allergy. The Uruguay delegates, who

had studied extrapulmonary tuberculosis only in adults, observed fifty-seven cases (6.69 per cent) of extrapulmonary infection out of 852 cases of pulmonary tuberculosis. This is in accord with general experience. They concluded from the rarity of extrapulmonary lesions and the clinical and morphologic pictures that diffusion is hematogenic. Investigations made in Venezuela confirmed these observations.

Habana was chosen as the meeting place of the next congress, to convene in 1943. Dr. Juan J. Castillo, a Cuban delegate, was named as chairman. Subjects for discussion planned are the Value of BCG Vaccination, Initial Stages of Tuberculous Infections and Systematization of the Therapy in Pulmonary Cavities.

Marriages

LIEUTENANT COMMANDER JOHN MATTHEW BACHULUS, M.C., U. S. Navy, to Mrs. Grace Adams East of Oakland, Calif., October 21.

JAMES BENJAMIN SHULER, Shenandoah, Va., to Miss Mary Catherine McCarthy of Butte, Mont., in Waikiki, Hawaii, August 31.

LOUIS WILLIAMS LADD JR., Cleveland, to Miss Barbara Schutz of San Antonio, Texas, at Mount Washington, Md., September 7.

RICHARD E. EDMONDSON, Hartford, Conn., to Miss Virginia Gholson of Clarksville, Tenn., in Nashville, Tenn., in September.

GRACE HUMPHREYS HOOD, Fort Worth, Texas, to Mr. Derwood Morton of Arlington in Dallas, September 12.

KENDRICK McCULLOUGH, Yonkers, N. Y., to DR. MARGARET WHITTAKER LAWRENCE of New York, November 8.

RUTH F. WOLCOTT, Spirit Lake, Iowa, to Mr. Otto William Fischer of Okoboji at Clear Lake, September 29.

BEN ALLEN DREIBOOT, Jacksonville, Fla., to Miss Norma Elizabeth Thomas in Augusta, Ga., October 7.

MILBURN H. QUERNA, Spokane, Wash., to Miss Patty Paxton of Springdale, in Lewiston, Idaho, October 3.

EUGENE J. MAIRE, Vail, Iowa, to Miss Betty Jane Van Ackeren of Humphrey, Neb., September 17.

BROWN McILVAINE DOBYNS, Jacksonville, Ill., to Miss Meredith Davis of Evanston in September.

OWEN M. CARROLL, New Castle, Ky., to Elizabeth Giles Thomas at Mount Sterling in October.

SHEPARD A. BURROUGHS to Miss Eleanor Mahan Hubbard, both of Ashtabula, Ohio, in October.

EINAR A. LUNDBURG, Hartford, Conn., to Miss Dorothy A. Oldfield in Burlington, Vt., June 15.

THOMAS BRICE MITCHELL to Miss Sara Elizabeth Tyson, both of Shelby, N. C., November 3.

JACK GRAHAM WEBB, Richmond, Va., to Miss Frances Skelton at Louisville, Ky., September 21.

H. FREDERICK KEIBER to Miss Marie Julian Hollan, both of Staten Island, N. Y., August 30.

ROBERT A. COEN to Miss Margaret Kernan, both of Ingleside, Neb., at Hastings, August 28.

WILLIAM J. SCHNUTE, Ann Arbor, Mich., to Miss Doris Davis of Lansing, June 29.

WENTWORTH L. OSTEEN to Miss Kate Elaine Goodson, both of Augusta, Ga., August 3.

ROBERT H. WAHL to Miss Florence Edith Hagedorn, both of Dayton, Ohio, in October.

LAD J. KUCERA, Lonsdale, Minn., to Miss Ethel Irene Benson in Omaha, September 28.

GILBERT D. KEIL, Toledo, Ohio, to Miss Carol Hoesman of Woodville in October.

LAWRENCE E. HURT to Miss Louise Conlee, both of Lexington, Ky., October 28.

LEONARD KLEIN to Miss Evelyn Rotkowitz, both of New York, November 9.

J. SAMUEL BLAIR, Gastonia, N. C., to Miss Mary Gwynne Fewell in October.

JORGE A. TRELLES to Miss Conchita Gonzalez, both of Tampa, Fla., in October.

Deaths

Carl Lucas Alsberg, Berkeley, Calif.; Columbia University College of Physicians and Surgeons, New York, 1900; assistant in physiologic chemistry, Harvard Medical School, Boston, from 1902 to 1905 and instructor of biochemistry from 1905 to 1908; chemical biologist, bureau of plant industry, United States Department of Agriculture from 1908 to 1912, and chief, bureau of chemistry, from 1912 to 1921; director of the food research institute, Stanford University, from 1921 to 1937 and, since 1937 consultant; dean of graduate studies at Stanford University from 1927 to 1933; since 1937 director of the Giannini Foundation of Agricultural Economics at the University of California; during the World War was chief chemist for the department of agriculture in the War Industries Board; member of the advisory committee on land utilization of the National Resources Planning Board; member of the American Society of Biological Chemists, of which he was a former president, American Chemical Society, for which he was a councilor and associate editor of its journal, and the Washington Academy of Sciences, of which he was a former president; aged 63; died, October 31, in the Alta Bates Hospital of pneumonia.

John Augustus Hartwell, New York; Yale University School of Medicine, New Haven, Conn., 1892; professor of clinical surgery emeritus at Cornell University Medical College, where he was for many years associate professor of surgery and professor of clinical surgery; president of the New York Academy of Medicine from 1929 to 1932 and director from 1934 to 1938; was an associate director of the American Society for the Control of Cancer; member of the Medical Society of the State of New York, the American Surgical Association and the Society of Clinical Surgery; fellow of the American College of Surgeons; served during the World War; consulting surgeon, Bellevue, Reconstruction, Presbyterian, Memorial and Lincoln hospitals, New York, Lawrence Hospital, Bronxville, and United Hospital, Port Chester; aged 71; died, November 30, in Oakdale, N. Y., of pulmonary embolism.

Henry Hurd Rusby, Sarasota, Fla.; University of the City of New York Medical Department, 1885; member of the Medical Society of New Jersey; professor of botany, physiology and materia medica, College of Pharmacy, Columbia University, New York, from 1888 to 1930 and dean from 1904 to 1930; professor of materia medica, University and Bellevue Hospital Medical College, New York, from 1897 to 1902; president of the American Pharmaceutical Association, 1909-1910; pharmacognosist in Bureau of Chemistry, United States Department of Agriculture, from 1912 to 1917; was awarded the Remington Medal of the American Pharmaceutical Association in 1923; author of numerous books; aged 85; died, November 18, of intestinal obstruction.

Joseph Nelson Davis ☉ Twin Falls, Idaho; Kansas Medical College, Medical Department of Washburn College, Topeka, 1907; served as secretary-treasurer of the Idaho State Medical Association from 1922 to 1931, when he was made president-elect, from 1935 to 1938 councilor and in 1938 again elected secretary-treasurer, serving until this year, when he asked to be relieved; served during the World War; on the staff of the Twin Falls County General Hospital; state chairman for the Committee on Medical Preparedness of the American Medical Association; aged 58; died, November 5, of injuries received in an automobile accident.

Frank Eliot West, Brooklyn; Long Island College Hospital, Brooklyn, 1876; professor of materia medica and therapeutics and clinical medicine at his alma mater from 1886 to 1921 and since 1921 emeritus professor of therapeutics and clinical medicine; member of the Medical Society of the State of New York; censor in 1878, vice president in 1890, president in 1891 and trustee from 1892 to 1902 of the Kings County Medical Society; served at various times and in various capacities on the staffs of the Kings County Hospital, Long Island College Hospital and the Brooklyn Hospital; aged 90; died, November 21.

Willard D. Duckworth, New Rochelle, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York; 1909; member of the American Roentgen Ray Society and the Radiological Society of North America; at one time assistant professor of roentgenology at the New York Post-Graduate Medical School, Columbia University; aged 57; on the staffs of the New Rochelle (N. Y.) Hospital, Tarrytown (N. Y.) Hos-

pital, Grasslands Hospital, Valhalla, and the White Plains (N. Y.) Hospital, where he died, November 11, of cerebral hemorrhage.

Frank Newton Irwin, White Plains, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; member of the Medical Society of the State of New York; adjunct professor of ophthalmology at the New York Post Graduate Hospital and Medical School from 1902 to 1907; consulting ophthalmologist, Manhattan Eye, Ear and Throat Hospital, New York; New York Hospital, Westchester Division, White Plains Hospital, St. Agne Hospital, Westchester Division, St. John's Riverside Hospital, Yonkers; aged 75; died, November 11.

Leonard Knight Graves, Elmhurst, N. Y.; Columbian University Medical Department, Washington, D. C., 1885; Bellevue Hospital Medical College, New York, 1887; member of the Medical Society of the State of New York; veteran of the Spanish-American and World wars; formerly an inspector in the New York Health Department; for many years on the staff of the New York Eye and Ear Infirmary, New York; aged 84; died, November 12, in the Veterans Administration Facility, New York.

David Sturges Fairchild Jr. ♂ Colonel, United States Army, retired, New York; Drake University Medical Department, Des Moines, 1897; veteran of the Spanish-American and World wars; was commissioned a lieutenant colonel in the medical corps of the regular army in 1920 and in 1930 a colonel; retired in 1935 for disability in line of duty; fellow of the American College of Surgeons; aged 69; died in November at Waynesboro, Va., of injuries received in an automobile accident.

Daniel Warwick Harmon, ♂ Colonel, M. C., United States Army, Hot Springs National Park, Ark.; University of Virginia Department of Medicine, Charlottesville, 1903; fellow of the American College of Surgeons; commissioned a first lieutenant in the medical corps of the army in 1909, a lieutenant colonel in 1929 and colonel in 1935; served during the World War; was commanding officer of the Army and Navy General Hospital; aged 60; died, November 8, of heart disease.

John King Freeman Ⓢ Louisville, Ky.; University of Louisville Medical Department, 1894; at one time adjunct professor of abdominal surgery and gynecology at his alma mater; past president of the Jefferson County Medical Society; veteran of the Spanish-American and World wars; aged 73; for many years on the staff of the SS. Mary and Elizabeth Hospital, where he died, November 6, of hypertrophy of the prostate, uremia and coronary sclerosis.

Edwin Charles Ebert ♂ Commander, United States Navy, Long Beach, Calif.; Marquette University School of Medicine, Milwaukee, 1916; was commissioned an assistant surgeon in the Medical Corps of the United States Navy in 1917, lieutenant in 1920, lieutenant commander in 1925 and commander in 1935; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; aged 50; died, November 4.

Joseph Thomas Buxton ♂ Newport News, Va.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the House of Delegates of the American Medical Association in 1920, 1922 and 1924; member of the Southern Surgical Association; fellow of the American College of Surgeons; surgeon in chief of the Elizabeth Buxton Hospital; aged 64; died, November 5, of coronary thrombosis and arteriosclerosis.

Joseph Augustus Crisler ♂ Memphis, Tenn.; Memphis Hospital Medical College, 1890; past president of the Shelby County Medical Society; member of the Southern Surgical Association and the Southern Society of Clinical Surgeons; fellow of the American College of Surgeons; aged 72; died, November 18, of cerebral hemorrhage.

Nov. 18, of cerebral hemorrhage.

Jay Harvey Bacon @ Peoria, Ill.; Johns Hopkins University School of Medicine, Baltimore, 1904; member of the Clinical Orthopedic Society; fellow of the American College of Surgeons; served during the World War; on the staff of the Methodist Hospital; formerly on the staff of the Proctor Hospital; aged 63; died, November 18, of arteriosclerotic heart disease.

James Andrew Brown * Commander, U. S. Navy, San Diego, Calif.; Ohio State University College of Medicine, Columbus, 1917; appointed assistant surgeon in 1917, promoted to the rank of lieutenant in 1920, lieutenant commander in 1925 and commander in 1935; aged 47; died, November 16, in the United States Naval Hospital of chronic myocarditis and nephritis.

Frank Taylor Andrews, Pasadena, Calif.; Chicago Medical College, 1884; member of the Illinois State Medical Society; professor emeritus of gynecology at his alma mater, now the Northwestern University Medical School; fellow of the American College of Surgeons; aged 82; died, November 7, of arteriosclerosis.

Percy Daniel Hoover ♂ Waynesboro, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; member of the board of trustees of Gettysburg (Pa.) College, and its secretary for many years; on the staff of the Waynesboro Hospital; aged 68; died, November 14.

Joseph Warrington Crawford ♂ North Adams, Mass.; Hahnemann Medical College and Hospital of Philadelphia, 1900; member of the Radiological Society of North America; on the staff of the North Adams Hospital; aged 68; died, November 7, of coronary sclerosis.

Byron Haskin, Theresa, N. Y.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1903; member of the Medical Society of the State of New York; since 1921 health officer of the consolidated health district of Theresa; aged 68; died, November 7.

Clark Wilder Hawley ♂ Chicago; Rush Medical College, Chicago, 1885; an Affiliate Fellow of the American Medical Association; member of the American Academy of Ophthalmology and Otolaryngology; aged 85; died, November 1, in La Grange, Ill.

Frederick Lincoln Emerson ♂ Boston; Boston University School of Medicine, 1892; served in various capacities on the staff of the Massachusetts Memorial Hospitals; for many years on the staff of the Brooks Hospital, Brookline; aged 78; died, November 10.

Siegfried Jackson, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; member of the Illinois State Medical Society; on the staff of the Columbus Hospital; aged 65; died, November 6.

Nellie Calista Flint, Mount Pleasant, Iowa; Hahnemann Medical College and Hospital, Chicago, 1899; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; aged 74; died, November 3.

William Francis Cunningham ♂ New York; Yale University School of Medicine, New Haven, Conn., 1911; served during the World War; on the staff of the Roosevelt Hospital; aged 51; died, November 19, in the Doctor's Hospital.

Joel Herbert Carter, Castleberry, Ala.; University of Alabama School of Medicine, 1910; member of the Medical Association of the State of Alabama; member of the county board of education; aged 59; died in November.

Samuel Scott Blacklock ♂ Hibbing, Minn.; Rush Medical College, Chicago, 1901; fellow of the American College of Surgeons; medical superintendent of the Rood Hospital; aged 66; died, November 12, of coronary thrombosis.

John Joseph Kenney ♂ Providence, R. I.; Dartmouth Medical School, Hanover, N. H., 1908; on the staffs of St. Joseph's, Homeopathic and Lying-In hospitals; aged 56; died, November 7, in the Jane Brown Hospital.

David Wendell Eames, Kecoughtan, Va.; University of the South Medical Department, Sewanee, Tenn., 1908; on the staff of the Veterans Administration Facility; aged 54; died, November 9, of coronary occlusion.

Mary Jardine Evans, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1935; member of the Medical Society of the State of Pennsylvania; aged 44; died, November 6, of tuberculosis.

Jean Girouard, Longueuil, Que., Canada; School of Medicine and Surgery of Montreal, Que., 1879; member of the legislative council from 1899 to 1937; formerly school commissioner; aged 84; died, November 12.

Michael Scott Kearns, Fort Lauderdale, Fla.; St. Louis University School of Medicine, 1926; formerly coroner of Hamilton County, Ohio; served during the World War; aged 40; died, November 14.

Tom Morford Throckmorton, Chariton, Iowa; Jefferson Medical College of Philadelphia, 1877; member of the Iowa State Medical Society; aged 88; died, October 31, in Des Moines of myocarditis.

Thomas Wayne Hancock, Lufkin, Texas; National University of Arts and Sciences Medical Department, St. Louis, 1913; aged 59; was killed, November 4, in an automobile accident.

Robert McKay Greenshields ♂ Romeo, Mich.; Detroit College of Medicine, 1900; served during the World War; aged 67; died, November 15, in the Jennings Hospital, Detroit.

James Henry Maynard ♂ Adair, Iowa; Rush Medical College, Chicago, 1899; past president of the Cass County Medical Society; aged 67; died, October 18, of acute myocarditis.

Gustavo Testa, Waterbury, Conn.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1902; aged 61; died, October 23, of coronary sclerosis and myocarditis.

John W. Barber, Yokena, Miss.; Kentucky School of Medicine, Louisville, 1884; aged 90; died, November 2, at Edwards of chronic myocarditis, hypertrophy and arteriosclerosis.

Nat Taylor Dulaney Jr., Bristol, Tenn.; Tennessee Medical College, Knoxville, 1893; aged 70; died, November 15, in the King's Mountain Memorial Hospital, Bristol, Va.

Simon Jay Mason, New York; University of Cincinnati College of Medicine, 1936; member of the Medical Society of the State of New York; aged 31; died, November 12.

Albert George Jenner, Milwaukee; University of Pennsylvania Department of Medicine, Philadelphia, 1897; served during the World War; aged 64; died, November 10.

Frederick Hubert Ladd, Canton, N. Y.; Albany (N. Y.) Medical College, 1902; member of the Medical Society of the State of New York; died, October 19.

Taylor Boyd Dixon, Washington, D. C.; Columbian University Medical Department, Washington, 1900; aged 64; died, November 2, of coronary thrombosis.

Robert James Baird, Creston, Ohio; Western Reserve University Medical Department, Cleveland, 1885; aged 87; died, November 3, of cerebral sclerosis.

Timothy Deason, Brachfield, Texas (licensed in Texas under the Act of 1907); aged 84; died, November 5, of heart disease and hypertrophic arthritis.

Harvey Baker Powers, Saranac Lake, N. Y.; University of Pittsburgh School of Medicine, 1920; aged 45; died, October 18, of pulmonary tuberculosis.

Frank Le Count Dowe, New York; New York Homeopathic Medical College and Flower Hospital, New York, 1889; aged 73; died, November 18.

Frank Leonidas Hall, Hannibal, Mo.; Rush Medical College, Chicago, 1887; at one time member of the state legislature; aged 79; died, November 11.

William Wirt Harvey, Boston; Harvard Medical School, Boston, 1898; member of the Massachusetts Medical Society; aged 74; died, November 10.

William Marshall Hinkle, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1891; aged 77; died, November 21.

Albert A. Duclos, Wisconsin Dells, Wis.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1895; aged 79; died, November 4.

Alvin Gustav Berger ♂ Chicago; Eclectic Medical College, Cincinnati, 1916; on the staff of the Grant Hospital; aged 48; died, November 9.

Morris Fallick, New York; Eclectic Medical College of the City of New York, 1905; aged 55; died, November 13, in the Lebanon Hospital.

Samuel Lumpkin Starks, Washington, D. C.; Howard University College of Medicine, Washington, 1920; aged 60; died, October 28.

Irving Edwin Burtnette, Morrice, Mich.; Hahnemann Medical College and Hospital, Chicago, 1898; aged 72; died, November 16.

Robert Tinion Hodgson Jr., Wilkinsburg, Pa.; University of Pittsburgh School of Medicine, 1924; aged 41; died, November 6.

Robert Nelson Buckmaster, Pangburn, Ark.; Gate City Medical College, Dallas, Texas, 1907; aged 71; died, November 17.

Thomas J. Hendrick, Webster, Ky.; Kentucky School of Medicine, Louisville, 1883; aged 80; died, November 6.

Charles J. Ayres, Newbern, Ala.; Medical College of Virginia, Richmond, 1886; aged 70; died, November 12.

Claude Bell, Tuscaloosa, Ala.; Chattanooga (Tenn.) Medical College, 1904; aged 64; died, November 3.

Ernst Theodor Hein, Palouse, Wash.; Baltimore Medical College, 1888; aged 84; died, October 3.

Bureau of Investigation

TWO FRAUDULENT "DIABETES CURES"

The Post Office Department has in the past debarred some "diabetes cures" from the mails, properly taking the stand that anything sold as an immediate or gradual substitute for insulin is an obvious fraud, and particularly dangerous when recommended for self treatment of the condition.

Dr. Samuel E. Edmunds' Concern

From Charleroi and Jeannette, Pa., Samuel E. Edmunds, M.D., and N. Edmunds, described as his wife, put out a mail-order nostrum, "Diabeto." It is said that Dr. Edmunds started the enterprise in 1938, renting a postoffice box at Jeannette, Pa., and doing business under his wife's name for what he called "ethical reasons." This is a timeworn excuse given by renegade physicians who hope to escape notoriety for their quackery by keeping their identities under cover.

"N. Edmunds" advertised that a "New German Remedy" for diabetes was "giving wonderful results" and that a six weeks supply could be had for \$5. Readers who responded received personal letters urging the purchase of Diabeto and advising that by the use of it "many" diabetic patients "get away" from the use of insulin. Also there was a questionnaire to be filled out, on the basis of which the customer was to receive "personal" advice on his case.

These facts were brought out in the memorandum submitted on the matter by Judge Vincent M. Miles, Post Office Solicitor. This document went on to show that persons who returned the questionnaire with the information that they had long been afflicted with sugar diabetes and were under physicians' care involving the use of a restricted diet and the injection of from 15 to 30 units of insulin daily, and who ordered Diabeto on the express basis that it be sent them if it would rid them of diabetes and enable them to discontinue dieting and using insulin, were furnished with Edmunds' nostrum.

Also it was shown that, instead of "personal" advice, Edmunds sent all remitters only stereotyped letters advising them to eat slowly, chew their food well, and purchase laxatives such as citrate of magnesia, Sal Hepatica, Glauber's salt and sodium phosphate. *There were also mimeographed dietary sheets that forbade the use of a wide variety of foods, although Edmunds had led customers to believe that by the use of his treatment they could return to a normal diet. Further, although before they purchased it he had claimed that it would enable them to discontinue taking insulin, after they had undertaken his treatment he advised them to continue using insulin indefinitely.*

Edmunds was quoted as saying that his product was based on a German compound, "Sepdelen," of which he claimed to have heard through an individual who allegedly had recovered from diabetic leg ulcers through the use of Sepdelen. The memorandum brought out that Diabeto was essentially a mixture of four of the sodium salts—the sulfate, tartrate, citrate and phosphate, all common saline laxatives. It also emphasized that it is necessary for a person with diabetes to follow a carefully weighed and balanced diet, with routine injection of insulin, and that there is no drug or combination of drugs known to medical science that is a satisfactory substitute for insulin. It was further pointed out that neither Diabeto nor any other drug nor combination of drugs was known to science as being capable of restoring to normal health the cells of the pancreas gland which have been damaged, atrophied or destroyed. On the contrary, it was shown that a product like Diabeto would injure the patient by keeping him in a state of constant laxation which not only would not control the amount of sugar and other toxins present in his blood but would also debilitate him because of continued loss of minerals and other nutritive substances through the bowels.

As the promoters of the scheme were unable to offer any scientific evidence to support their claims for Diabeto, the solicitor recommended that a fraud order be issued against the names under which they did business—N. Edmunds, Samuel E. Edmunds, M.D. and S. E. Edmunds, M.D. at Charleroi and Jeannette, Pa. It was issued on Dec. 13, 1939.

A Dr. S. E. Edmunds who may have been the person mentioned was listed as "Medical Counselor" on a letterhead of Lee & Company, Philadelphia, that was sent out in August 1939, accompanied by a circular showing that the Lee concern was advertising "Fru-min Salts, formerly German Fruit Salts," also described as "The New Bio-Chemical Therapy for acute, chronic, lingering diseases, treating the CAUSE, composed of 13 remedies, 39 strengths." Although the stuff, from the claims and testimonials cited, purported to be something of a cure-all, the circular declared "We specialize in diabetes." The fact that it was also represented to come from Europe indicates that it may have been identical with or similar to the Sepdelen or Diabeto that has been mentioned.

The circular in question bore the rubber stamp of H. Landgraf, Philadelphia. THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION for Oct. 27, 1934, carried an article detailing the case of a Post Office fraud order issued against H. Landgraf and his "German Fruit Salts," represented as a veritable cure-all and especially played up for diabetes. The article also brought out that Landgraf was then apparently trying to circumvent the fraud order by putting out a diabetes nostrum under the trade style of "Hilton Chemical Company" at Philadelphia.

Samuel Ernest Edmunds appears in the American Medical Association's records as a graduate of the Atlantic Medical College, Baltimore, in 1910 (the year it became defunct) and as obtaining, in the same year, licenses to practice in Pennsylvania and Maryland, the latter issued by the homeopathic board. He is not shown as a member of his local medical society.

National Diabetic Food Company

Under the foregoing title and also the name "National Diabetic Food Company" a George H. Keys and an R. Randall put out from Kansas City, Mo., "National Diabetic Food" and "National Mineral Ration." The Post Office Department's investigation revealed that these promoters had been in the "diabetes cure" game since 1936, though neither possessed any medical training or experience, nor was any one with such qualifications connected with the company.

Victims were lured by such advertising claims as:

No matter how bad or how long you have suffered, you can now get a treatment that has relieved some of the worst cases we have seen. No drugs or complicated directions. . . .

To persons who "bit" the concern sent printed form letters containing such preposterous misrepresentations as that the causes of diabetes prevail in over two thirds of the American homes and that the remedy lies in National Diabetic Food and its accessory product, National Mineral Ration, through the use of which a person with diabetes would be able to resume a normal diet and gradually quit the use of insulin altogether.

Judge Vincent M. Miles, Solicitor for the Post Office Department, brought out in his memorandum on the case that National Diabetic Food was pulverized and prepared for sale by the promoters in their homes from a weed called saltbush, which they obtained at no cost from farms around Kansas City. Chemical and microscopic analysis in government laboratories showed that it was composed essentially of traces of calcium, iron, phosphate, sodium, potassium and chloride in the form of plant ash.

Similar analysis of National Mineral Ration, the supplementary product which the concern obtained from an Indianapolis concern, revealed that it was essentially composed of minute amounts of epsom salt, calcium, iron, manganese, sodium, potassium, ammonia, carbonate, bicarbonate, sulfate, chloride and sulfur, with traces of iodides, bromides and possibly of copper, zinc and lithium.

The solicitor's memorandum declared that these mixtures, whether used singly or in combination, were absolutely worthless for treating diabetes, a condition due to lack of insulin, a hormone normally secreted by special cells of the pancreas gland which are known as the "islands of Langerhans." The memorandum went on to show that diabetes is characterized by the faulty metabolism of sugars, fats and starches, and the presence of excess sugar, acids and other toxic bodies in the blood and urine; that diabetes is incurable but may be effectively controlled, and blood sugar kept at a normal level by constant use of a

carefully weighed and balanced diet; and that in addition to stringent dietary measures severe cases require routine injections of insulin to compensate for the body deficiency therein.

Further, evidence was presented to show that certain diabetic patients who were treated with saltbush lapsed into diabetic coma both while taking and shortly after they had ceased using it, and that the prolonged use of it had resulted in the deaths of some such patients.

An interesting sidelight on the case was brought out in the revelation that the wife of one of the promoters had died of diabetes while taking these nostrums, which fact he admitted, though he attributed her death to her failure to follow a proper diet. Another feature of the hearing was the defendants' claim that their National Mineral Ration had been analyzed and passed by the Indiana State Board of Health, whereas the Post Office presented information from that board that this claim was untrue.

The conclusion of the solicitor was that there was sufficient evidence that the business was a scheme for obtaining money illegally through the mails, and he recommended the issuance of a fraud order. This was issued on Feb. 1, 1940, against the names National Diabetic Food Co., National Diabetic Food Company, National Diabetik Food Company, Geo. H. Keys, Ps.D., R. Randall, and their officers and agents as such.

The concern, however, like many other outfits that have perpetrated swindles by mail, simply changed its name and continued to do business. In a new memorandum issued by Judge Miles on May 28, 1940, he said of this scheme, in part:

Evidence now before me shows that George H. Keys, in an attempt to evade the effect of the fraud order against the National Diabetic Food Company enterprise, has adopted the assumed and fictitious title of Natur-Food Company, under which name form letters and mimeographed circular matter are being sent through the mails to former customers and others advising them that further purchases of "National Dibetik Food" and "National Minral Ration" may be made from the Natur-Food Company and furnishing a business reply envelope addressed to Natur-Food Company, P. O. Box 2623, Kansas City, Missouri, for that purpose. One of these form letters, on the letterhead of "Tru-Science," reads in part as follows:

Dear Friend: * * *

It seems that a technical error has arisen which is causing the NATIONAL DIBETIK FOOD COMPANY considerable trouble. They believe that, because of the nature of the information that is given out to the public, a large national association is behind this action.

The NATUR-FOOD COMPANY IS HANDLING NATIONAL DIBETIK FOOD, NATIONAL MINRAL RATION AND ELECTREAT MECHANICAL HEART. The same offers, prices and information are available. In ordering, ORDER FROM—

NATUR-FOOD COMPANY

P. O. Box 2623

Kansas City, Mo.

Save this address for future correspondence. MAKE ALL CHECKS AND MONEY ORDERS PAYABLE TO NATUR-FOOD COMPANY. Miss Velma L. Hanson is in charge of the NATUR-FOOD COMPANY and will extend you the same courteous and prompt service that has been the policy of the NATIONAL DIBETIK FOOD COMPANY to give its many customers throughout the nation. The NATUR-FOOD COMPANY will be very pleased to have you order from them. * * *

The evidence further shows that the preparations "National Dibetik Food" and "National Minral Ration" have actually been sold through the mails by Natur-Food Company in response to an inquiry addressed to that concern specifying that the products were desired for use by a diabetic sufferer in place of insulin. Accompanying the preparations was a mimeographed treatise upon the history and alleged value of saltbush (National Dibetik Food) if used continuously, in the treatment of mild, severe, long-standing and gangrenous cases of diabetes. This article bears the signature of T. R. Randall, one of the promoters of the original National Diabetic Food Company enterprise. Attached to this dissertation was a series of mimeographed questions and answers on the subject of the use of saltbush.

The evidence before me shows, and I so find, that this is a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises and is an evasion of the fraud order of February 1, 1940.

While it appears that the name "Tru-Science" is also used in certain instances in such a manner as to imply some connection with the Natur-Food Company, inasmuch as persons solicited are directed to make all checks and money orders for the products purveyed herein payable to the latter concern, it is believed that the extension of the fraud order of February 1, 1940, to cover the name Natur-Food Company only will effectively suppress this scheme.

I therefore recommend that a supplemental fraud order be issued against Natur-Food Company, Natur-Food Co., and their officers and agents as such, at Kansas City, Missouri.

This order was issued on May 28, 1940.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

CARDIAC ACTIONS OF QUINIDINE AND DIGITALIS

To the Editor:—While reading the article by Dr. Levy on cardiac arrhythmia in the Sept. 7, 1940, issue of *The Journal* I encountered an old problem of mine. I cannot get a consensus about the comparative actions on the myocardium, auriculoventricular conduction and so on of quinidine and digitalis. In fact, many of the standard textbooks appear to contradict one another in the application of the principles of what these drugs are said to do. The matter has caused considerable argument among my friends and I would appreciate some information on the matter.

M.D., Tennessee.

ANSWER.—Digitalis and quinidine are both valuable remedies for patients with cardiac disease but each has its elected place in cardiac therapy. When each drug is properly used and the limits of its actions are known and its specific indications recognized, much benefit may be expected.

Quinidine, a protoplasmic poison, is known to act directly on the myocardium. It decreases its irritability. It also is known to depress auriculoventricular conduction and to prolong the rate of intraventricular conduction. Although the actual refractory period of auricular muscle may not be prolonged, as pointed out by Love, it is the opinion of Lewis and Drury that the effective refractory period is prolonged by delay of the spread of the impulse through the auricular muscle. It produces vagal depression and occasionally by slowing the rate of the fibrillating auricle it also acts to increase the ventricular rate. It is known that, in 60 per cent of cases of auricular fibrillation, quinidine has been successful in restoring normal sinus rhythm. It is apparently most successful in the cases of fibrillation of short duration or of the paroxysmal type, although it is also occasionally effective in cases of many years' duration. It is least valuable in instances of fibrillation associated with severe cardiac insufficiency and it is here that it has its greatest dangers. It is now believed that it should not be used for patients with marked cardiac disease or auricular fibrillation of many years' duration associated with cardiac enlargement, because of the possibility of producing cardiac standstill. Premature auricular systoles, occurring singly or in short runs, are usually depressed by the use of quinidine. Ventricular extrasystoles, if causing undue symptoms and when not the result of extracardiac mechanisms, may occasionally be quieted with quinidine. The presence of frequent premature ventricular systoles in instances of recent myocardial infarction warrants the use of quinidine to prevent the possible occurrence of ventricular tachycardia and fatal ventricular fibrillation. Occasionally quinidine has been used intravenously in instances of ventricular tachycardia and short runs of ventricular fibrillation, but because of possible peripheral circulatory collapse and drop in blood pressure and also further depression of the conducting tissues it should be used only with great caution. Because of its action in reducing the irritability of the myocardium and in prolonging the intraventricular conduction time, the drug should not be used for patients with marked degrees of block in the conducting system. Because of its peculiar properties as enumerated, it is evident that quinidine has certain definite indications and also contraindications, and these should be fully understood before quinidine is administered.

Digitalis has certain definite known actions on the cardiac mechanism which are well stated in the standard textbooks. It is known definitely to have a selective action on the conduction system, especially the auriculoventricular node, and when used beyond therapeutic dosages it will give rise to bizarre ectopic rhythms and ultimate ventricular fibrillation if not stopped. Together with its stimulating action on the vagus nerve and depression of auriculoventricular conduction, it has been used to slow the ventricular rate and maintain it at a slow rate in auricular fibrillation. Gold and his associates have recently shown that the vagal factor predominates in such instances with moderate digitalization, while the extravagal factor predominates after larger doses. The apparent discrepancy of the action of digitalis in sinus rhythm as contrasted with auricular fibrillation in slowing the ventricular rate is not clearly understood at present. However, the presence of congestive failure, with either sinus rhythm or auricular fibrillation, is an indication for the use of digitalis. In contrast to quinidine, digitalis increases the contractility of the heart. The exact mechanism by which

digitalis does this is not fully explained at present. The one constant effect of the drug is to cause a diminution in cardiac size in normal animals and man and in patients with congestive heart failure. Some investigators have explained this as a consequence of its direct action on the myocardium with varied results. The prevailing theories are that there may be an increase in tone, an increase in systolic force or a decrease in the diastolic length of the individual muscle fibers. Others have attributed its beneficial actions to a peripheral circulatory action by pooling the venous blood in the liver channels, thus decreasing the size of the heart and allowing for more efficient contraction. Discussion of the experimental evidence is not pertinent at this time, but, whatever the exact action may be, digitalis helps to relieve congestive heart failure.

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TREATMENT OF TUBERCULOSIS IN NEGROES

To the Editor:—The superintendent of a tuberculosis sanatorium recently stated that collapse therapy (pneumothorax) is inadvisable when the patient is a Negro. He maintained that this is the consensus in leading tuberculosis institutions, citing in particular Bellevue Hospital in New York City. Is belonging to the Negro race now considered a contraindication to collapse therapy in pulmonary tuberculosis? Can you furnish any references on the subject?

M.D., New York.

ANSWER:—At one time it was believed that no treatment was of any avail for Negro patients. This probably was due to the fact that Negroes usually did not report for examination until their disease was too advanced for treatment to be of any benefit. In more recent times, however, there has been much health education work done among Negroes, which has encouraged at least some of them to be examined while apparently in good health. Negro nurses and physicians are doing a great deal of this educational work. Many clinics have been established for those with little or no financial means, which have made examinations readily available. Surveys have been conducted which include examinations of healthy appearing Negroes. These and other activities have resulted in finding tuberculosis in earlier stages when symptoms are present and in the presymptom stage in many cases. Thus, large numbers of Negroes are having tuberculosis detected at a time when it is treatable.

Some workers are of the opinion that the Negro develops a different type of tuberculosis than the Caucasian—a more rapidly progressive type. They are of the opinion that this may be due to lack of immunity; others, however, contend that the Negro does not develop a different type of tuberculosis than the Caucasian but that his exposure often is of such a nature that so many tubercle bacilli are admitted to his body as to produce overwhelming and rapidly progressive disease. In either event, the Negro who does not have hopelessly advanced tuberculosis may have his lesions treated with great success and by the same methods as are employed in the treatment of the Caucasian.

Collapse therapy has been and is being used extensively in the treatment of tuberculosis among Negroes. The procedure of choice is artificial pneumothorax, but when, by reason of adhesions, this cannot be accomplished, surgical procedures, especially extrapleural thoracoplasty, are indicated and have been practiced with remarkable success.

Chadwick, Markoe and Thomas (*Am. Rev. Tuberc.* **28**: 759 [Dec.] 1933) reported the results of treatment of 464 Negroes who had pulmonary tuberculosis. They were all on strict bed rest, and collapse therapy was used in 70 per cent. They divided their patients into light, medium and dark skinned groups. While the results of treatment were a little better in the light skinned group, a higher percentage of improved cases was found in the dark than in the medium group. They concluded that the degree of color is not particularly significant. They produced an excellent record for treatment among these Negroes when one considers that in 90 per cent of the patients the disease had advanced beyond the minimal stage before treatment was instituted.

Brock (*ibid.* **28**: 767 [Dec.] 1933) reported the results of his collapse therapy work on thirty-six tuberculous Negro patients, all of whom were in the advanced stage of the disease when

treatment was begun. Thus he started with a serious handicap. Therefore only 17 per cent were improved or restored to working capacity.

Gaines and Keller (*ibid.* **28**: 779 [Dec.] 1933) also treated Negro patients by collapse therapy and came to the conclusion that the results approximate those obtained in the white race closely enough to reward the physician for his effort and the patient for his cooperation in submitting to this form of treatment. They consider artificial pneumothorax as the procedure of choice, although extrapleural thoracoplasty was used in some cases. With few exceptions they believed that the indications for collapse therapy in the Negro race should be identical with those of other races and the results obtained in their hospital compared favorably with results reported among combined races.

Since these reports were made, large numbers of Negroes have been treated by collapse therapy with excellent results. In Puerto Rico J. Rodriguez Pastor has reported (*Journal-Lancet* **60**: 160 [April] 1940) that ambulatory artificial pneumothorax has been administered to more than 4,000 patients and pneumothorax has been used in large numbers of patients who are hospitalized. Negro patients receive artificial pneumothorax the same as those of other races and apparently with similar results.

Guild, who is director of the Negro program of the National Tuberculosis Association, travels extensively through the South and finds that collapse therapy is being used on Negroes in nearly all of the Southern states.

Therefore the Negro race is not now generally considered a contraindication to collapse therapy in pulmonary tuberculosis. Artificial pneumothorax is doing much not only to control tuberculous lesions in individual patients but also to convert positive sputum to negative and even prevent some patients from becoming contagious.

TOXICITY OF VINYLITE RESINS

To the Editor:—What are the industrial complications such as allergy and toxicity of a product used in dyeing shoes, namely "Vinylite."

Russel G. Means, M.D., Columbus, Ohio.

ANSWER:—"Vinylite" is the trade name for a series of vinyl compounds manufactured by the Carbide and Carbon Chemicals Corporation. This type of plastic may be produced in any color or in translucent and transparent forms. It is suitable for use as articles of personal wear such as belts, suspenders, garters and shoe tops and for dentures, phonograph records and splints and in coating materials. Although no information is available on the use of this type of resin as a shoe dye, patents have been awarded for its use as a coating for textiles. This use involves the addition of ancillary products such as plasticizers, solvents, stabilizers, dyes and inhibitors, which include known skin irritants and sensitizers. Claims have been made that vinyl compounds themselves are nontoxic; however, there still remains the possibility of injury from the other products present. The type of skin injury associated with these resins was described by Dr. Erwin P. Zeisler in *THE JOURNAL*, June 29, page 2540, in an article which refers to dermatitis from garters and wrist watch straps made from vinyl acetate and vinyl chloride. More recently, dermatitis from handling resin-lined tin cans has been reported (Schwartz, Louis, and Russell, J. P.: *Occupational Dermatitis from Handling Resin-Lined Tin Cans*, *THE JOURNAL*, Aug. 10, 1940, p. 448).

SOLUTION OF POSTERIOR PITUITARY FOR HERPES ZOSTER

To the Editor:—What is the rationale for the use of solution of posterior pituitary in the treatment of herpes zoster? I am treating a white man aged 31 with daily injections of 15,000 international units of thiamine hydrochloride. He has herpes zoster involving the ophthalmic division of the trigeminal nerve. The results are apparently good, the lesions crusted after the third injection and the pain has almost disappeared. I have spoken to some men who have used Vitamin B₁ in cases of herpes zoster and they report little success. However, their dosage was lower.

Sidney J. Kohle, M.D., Woodmere, N. Y.

ANSWER:—Somers and Pouppirt (*Herpes Zoster: Some of Its Clinical Aspects*, *California & West. Med.* **42**: 370 [May] 1935) have formulated a theory to explain the action of solution of posterior pituitary and epinephrine in relieving the pain of herpes zoster. Because of the fact that one of the chief changes in the tissues affected in this disease is vasodilatation, they suggest that it is the vasoconstricting action of these drugs that relieves pain in many cases. They differentiate two kinds of pain in zoster: (1) a stabbing, shooting pain, usually intermittent, along the segment or segments involved, usually not sharply localized, and (2) a sharply localized burning, itching or stinging pain at the site of the skin lesions or at the locality at which they are about to appear. Solution of posterior pituitary regularly relieved pain of the second kind

but was not always successful in the neuralgic pain of the first variety, a point in which their experience agrees with that of other writers.

Pillsbury and Fondé (The Treatment of Herpes Zoster, *M. Clin. North America* 20:239 [July] 1936) quote Somers and Pouppirt's theory and agree that it seems to them a reasonable explanation.

Flexner, Chassin and Wright in a recent article (Studies in Herpes Simplex Encephalitis in Rabbits, *J. Infect. Dis.* 66:30 [Jan.-Feb.] 1940) tried vitamin C, sulfanilamide and pitressin in the attempt to control the encephalitis of rabbits. In discussing the possible action of pitressin, they evidently included it in their experiment because of its use in the treatment of herpes zoster and although they apparently had not read Somers and Pouppirt's article they came to the same conclusion, that the drug probably acts by its vasoconstrictive power.

PROBABLE ARTHRITIS OF WRIST

To the Editor:—A girl aged 17 has been playing golf daily during the summer months for the past four years. Last year she developed a pain in the right wrist while playing and it bothered her off and on during the remainder of the summer. Rest for a few days has always relieved the pain. During the winter she practiced on the violin one hour or more daily without experiencing the slightest discomfort in her wrist. On June 1 she began playing golf again and got along well for four or five weeks. The pain then returned and has caused her a great deal of annoyance. The pain seems to be located in the second carpometacarpal, that is, the joint between the second metacarpal and the trapezoid. On examination and questioning I have noted the following points: 1. Pain occurs on pressure on the dorsal surface of the wrist over this joint. 2. Cocking of the wrist at the top of the back swing causes pain in this region. 3. After a round of golf, flexion and extension of the wrist cause pain. 4. Pressure on the palm of the hand as, for example, leaning on the arm with the palm of the hand resting on a table, causes pain. 5. Pressing together the index finger and the thumb as in holding a pen causes pain if done one or two hours after playing a round of golf. She has been instructed by three well known professionals and her form is considered good. An improper grip or faulty swing can probably be ruled out as a cause of the trouble. What can the cause of this pain be and what can be done to relieve it permanently?
M.D., West Virginia.

ANSWER:—The history suggests an arthritis. Presumably x-ray films have been made and carefully studied, although this is not mentioned in the letter. If the trapezoid and second metatarsal joint are clear and show no changes, it would be well to scrutinize closely the x-ray film of the proximal row of carpal bones of the wrist, paying particular attention to the semilunar bone, which occasionally is the seat of a noninfectious aseptic osteitis called Kienböck's disease.

All foci of infection should be searched for and eliminated. If the condition is an arthritis, rest is essential, even to the extent of giving up golf for a season. A cock-up wrist splint may be worn, which will keep at rest the various component joints of the wrist and still permit movement of the fingers. If this fails to give relief, consultation with an orthopedic surgeon would be advisable.

THUMB SUCKING IN INFANTS

To the Editor:—What is the attitude of pediatricians toward thumb sucking in infants and children? Should one attempt to stop them or let the habit run its course? Is it thought that dentition and oral development are influenced by thumb sucking? W. E. Oldham, M.D., Lebanon, Ky.

ANSWER:—The opinion of pediatricians is somewhat divided with regard to the proper handling of thumb sucking. Some believe that the habit should be completely ignored in all infants under a year of age. Others favor the use of some restraining device, such as pasteboard splints on the arms, aluminum mitts or other coverings for the hands. The application to the thumb of bitter substances is of service only in the milder cases and even in such instances may not be of benefit.

Few pediatricians are willing to accept the view that thumb sucking may have a sexual basis. Curtailment of the thumb sucking may lead to the development of some substitute habit. Thumb sucking is more liable to occur when a child is about to go to sleep or when he is hungry.

Opinions seem equally divided as to the effects of thumb sucking. Some orthodontists are inclined to believe that the continued sucking will lead to malocclusion and deformity of the jaw; others do not concur but rather consider the etiology of malocclusion to be based on heredity and other factors.

If the habit is unduly frequent or of a combined type, that is, accompanied by hair pulling, nose rubbing and the like, it is probable that efforts should be made to overcome the habit. Mechanical restraint probably is the most effective method of treatment in such cases. In milder cases in which the habit is of infrequent occurrence, it may well be ignored.

SYPHILITIC MYELITIS

To the Editor:—A white woman aged 56 complained on March 5, 1940, of paresthesias of the feet, legs and lower part of the abdomen. There was a burning sensation in the right foot beginning at the plantar surface of the second toe and running back along the medial half of the plantar surface of the foot and up the leg. There was a feeling of tightness about the lower part of the abdomen and back. With the onset of these symptoms in January 1940 there was difficulty in walking. The sensory disturbances were distressing at night. She had lost 10 pounds (4.5 Kg.) since the onset of her illness. The patient is intelligent and there is no loss of memory. Speech is not affected. There are no headaches, vertigo, or gastrointestinal complaints. The appetite is good. Menstruation ceased at the age of 51. Her past medical history is negative. She has been married for thirty-one years, has never been pregnant, and states that her husband, aged 71, is in good health. The patient weighs 105 pounds (47.6 Kg.). There are no abnormalities of the skin, eyes, ears, nose, throat or lungs. The pulse rate is 84. The blood pressure is 176 systolic, 90 diastolic. Abdominal and pelvic examinations are negative. The gait is unbalanced, faltering and ataxic. Falling is apt to occur if a cane is not used. The pupils react normally to light and in accommodation. The patient's eyes were examined by an ophthalmologist and no abnormalities whatever were detected. There is no tremor. The tendon reflexes at the wrist and elbow are normal. The superficial abdominal reflexes are absent. The knee jerks are hyperactive. The Babinski reflex is questionable. The Romberg test is positive. The finger to nose test is well done. The heel to knee test cannot be evaluated because of spasticity of both lower extremities (adductor spasm?). Thermal and tactile sensibility is impaired in both lower extremities, the degree of impairment increasing from above downward. The urine is normal. On March 18 the red blood cells numbered 3,510,000, the hemoglobin 80 (Sohli), white blood cells 9,750, the differential normal. The blood Kahn reaction March 18 was positive. Spinal fluid examination March 29 revealed normal pressure, the Wassermann and Kahn reactions negative, white cells 4, globulins moderately increased, total protein 150 mg., colloidal gold curve 1122210000. My diagnosis was neurosyphilis, probably with early myelitis involving the lower dorsal and lumbar regions of the cord. Since March 30 she has received ten injections of bismuth subsalicylate in oil followed by ten 2 Gm. doses of trypanamide and is now on a second course of the bismuth compound. She is taking potassium iodide orally (60 minims, or 3.7 cc., of the saturated solution daily) and tolerates her treatment well. To date there has been no improvement in her nervous symptoms, although there is no evidence of progression. The positive neurologic signs remain the same. The weight remains the same. A red blood cell count repeated on July 11 showed 4,040,000 with a hemoglobin of 88 per cent. Blood tests repeated at another laboratory July 15 revealed the Wassermann negative, Kahn 4 plus and Kline 3 plus. I would appreciate your opinion as to the diagnosis. I understand syphilitic myelitis to be a diffuse meningeovascular lesion of the cord with general softening, amounting to infarction. The clinical and laboratory observations in this case seem to fit this diagnosis, except for the normal spinal fluid cell count, which would speak against meningeal involvement. What treatment would you advise? What is the prognosis? What of fever therapy in this case, and when should it be given with reference to drug treatment?
M.D., Ohio.

ANSWER:—From the description, the patient's condition may be classified as a myelopathy or a myelitis; or, in view of the serologic test, the possibility of a vascular type of neurosyphilis must also be considered. A report of the jugular compression test and a report of x-ray examination of the thoracic spine would be of help in making a diagnosis. The first blood count report raised the question of a pernicious anemia, so further study of blood smears and a gastric analysis with histamine may be helpful.

The results of treatment of patients who have a syphilitic myelitis are quite unsatisfactory. In view of the patient's age and type of involvement, the continued use of trypanamide and a bismuth compound would seem warranted. The use of fever therapy in this type of case is attended with considerable risk and small chance of improvement.

ARTHRITIS OR SERUM ARTHRALGIA

To the Editor:—A man aged 45 had no joint symptoms until he was given serum for pneumonia in February 1940. He developed a serum sickness and continues to have stiffness and pain in practically all his joints. The joints are not deformed but are tender. Warm baths and salicylates have been of no value. Can you suggest any treatment that might help? There are no evident foci and he is otherwise in good health.
M.D., Indiana.

ANSWER:—It is unlikely that articular symptoms of several months' duration are related to serum therapy. The articular symptoms of serum sickness generally last not more than a few days, in the experience of Boots and Swift, not more than nine days in any one joint. In serum sickness there occur, two or three weeks after the serum therapy, fever, urticaria, sometimes enlargement of lymph nodes and, in many cases, pain and tenderness of the joints, less often actual redness and swelling of joints. Arthralgia, rather than arthritis, is usually present. Analysis of the synovial fluid may reveal an increased cell count and the presence of the offending antigen.

In view of the persistence of the patient's pains, he apparently has some condition other than the arthralgia of serum sickness. He is approaching the age when degenerative (hypertrophic)

arthritis and its accompanying muscular stiffness are common. The latter generally can be readily differentiated from chronic atrophic (infectious) arthritis by making roentgenograms and estimating the sedimentation rate.

References:

- Boots, R. H., and Swift, H. F.: The Arthritis of Serum Sickness, *THE JOURNAL*, Jan. 6, 1923, p. 12.
Hench, P. S.; Bauer, Walter; Dawson, M. H.; Hall, Francis; Holbrook, W. P.; Key, J. A., and McEwen, Currier: The Problem of Rheumatism and Arthritis, *Ann. Int. Med.* 13:1655 (March), 1937 (April) 1940.

UNUSUAL SYMPTOMATOLOGY IN PERIARTERITIS NODOSA

To the Editor:—A woman aged 40, single, with a definite diagnosis of periarteritis nodosa, was given an ampule of metaphyllin 0.24 Gm. in a 10 cc. solution intravenously. Two and a half hours later she became disoriented and failed to respond to questions, repeating "vomit, vomit" and sucking on her fingers. There is a question of a temporary amaurosis. The left pupil reacted to light (the right dilated and fixed from a previous episode of retinal hemorrhage and blindness). Physical examination was otherwise negative. One hour later I was called because of a clonic convulsion with frothing at the mouth and coma. There was no bowel or bladder incontinence. The pulse was full and bounding. There were no sibilant or sonorous rales, which had been present for years on and off and which were noted early that morning. Nikethamide was given intramuscularly. Slow and irregular respirations soon appeared, to become deeper and more regular. One and a half hours later I returned because of another similar convulsion. The condition was as before. Nikethamide was given again. The patient remained comatose for another two hours. At that time she stirred and turned on her side. She looked up, recognized me and spoke to me. There were still moist rales in her chest. She was still disoriented. Four hours later she responded to questions and made plans for her family and for her own diet for the following day. She thought she "was dry" but didn't care for any food that night although she sipped a little water. She slept well through the night. The following morning her appetite was poor. She felt exhausted. She had vomited some orange juice. Sibilant rales were noted throughout both lungs. There was an equivocal Babinski sign on the left and a weak left ankle jerk. The abdominal reflexes were lively except for the lower left quadrant. She remembered nothing since a faintness coming over her the previous day at the beginning of the episode until seeing me some eight hours later. The blood pressure was now 132/80 (from 170/94 of the previous day). She has been taking epinephrine, iodides, ephedrine, bromides and metaphyllin (by vein) as necessity required for a number of years. For the last month there has been slight weekly vaginal bleeding, which this day was more profuse (this has occurred previously after metaphyllin). For a number of days there has been numbness of the toes relieved by heat and elevation, and which is now gone. Is it possible to tell me what occurred? No air, I am sure, was injected. I would not care to use the drug again if there is any relationship, but she feels that it has always helped her in the past.

M.D., Connecticut.

ANSWER:—It seems unlikely that the drug was responsible for the train of symptoms described in this case. Metaphyllin is theophylline with ethylenediamine. Less than 0.2 Gm. of theophyllin is contained in 0.24 Gm. of the compound. This dose is well within the limits of safety, especially if the injection is given rather slowly. From one and one half to two minutes should be consumed in injecting the drug. The fact that the patient had received many such injections previously would rule out sensitiveness to the drug. In addition to this, patients who are sensitive react promptly and not two and a half hours later.

In a disease with such protean manifestations as periarteritis nodosa it is much more likely that the symptoms described were the result of the disease itself, probably a cerebral thrombosis or the rupture of a cerebral aneurysm.

DEPILATORY PASTE

To the Editor:—Is there any contraindication to the use of a depilatory paste containing barium sulfide on the face, the paste containing 4 drachms (15 Gm.) of barium sulfide and 2 drachms (8 Gm.) each of powdered zinc oxide and powdered starch? Is it advisable to reduce the average exposure time of from one to two minutes if such a paste is used on the face?

M.D., Illinois.

ANSWER:—The depilatory paste mentioned is one of the formulas of Duhring and must be thinly applied to the area to be treated and allowed to remain until there is a slight sensation of burning (not longer than one or two minutes) and then scraped off. Such a paste when used repeatedly on the face is apt to cause dermatitis and conjunctival irritation, in addition to being unpleasant to the sense of smell because of its sulfide content. Since the process must be repeated with the reappearance of the hairs, there is great likelihood of irritation (dermatitis venenata) on the face, and it is well, therefore, to reduce the exposure time to a minimum. Other methods of depilation, e. g. electrolysis, in proper hands is a safer and more permanent procedure for removing superfluous hair if the involvement is not too extensive.

STERILIZING ADHESIVE TAPE

To the Editor:—I have the problem of sterilizing adhesive tape which may not be put to immediate use but which may have to be stored for several months. Can you tell me what method I can use without impairing the adhesive qualities of the tape? Will exposure to short wave diathermy kill bacteria unless there is sufficient heat developed to effect also the sticking power of the adhesive? If so, what wavelength would be most effective?

M.D., New York.

ANSWER:—Exposure to short waves is at best an uncertain method of sterilization of adhesive tape, and subsequent packing for storage would add to the technical difficulties involved. Sterilization with moist heat is the method of choice. One firm of manufacturers (Johnson and Johnson, New Brunswick, N. J.) produces a tape which, it is stated, may be so treated without impairment of its adhesive qualities. Sterilizable tape should be faced, it is said, with crinoline or some other cloth. It must be so placed in the autoclave that steam can freely reach the entire surface; i. e., it should lie in separated flat strips or sheets or in a loose roll. The manufacturers recommend 10 pounds pressure (240 F.) for thirty minutes. A minor problem is to prevent excessive drying during the period of storage, which would impair the adhesive quality.

FUNCTIONAL POSITION IN ANKYLOSIS OF THE HIPS

To the Editor:—What is the optimal functional position in bilateral ankylosis of the hips?

M.D., Pennsylvania.

ANSWER:—Abduction of from 10 to 15 degrees of each leg with slightest degree of external rotation probably would be considered best in the average case. This produces the broadest base of support for walking. There are some instances in which one must give consideration to the individual case; namely, some people would rather have the hips stiff in flexion so that they can sit, rather than in extension, which is better for standing, walking and lying. A court reporter may prefer the sitting position.

Another factor is the amount of movement possible in the lumbosacral area. Unfortunately so many victims of bilateral ankylosis have in addition ankylosis of the sacro-iliac and lumbosacral joints that they have no outlet in the lower back area to compensate in any measure whatever for the stiffness of their hips. Occupation and marital relations are important factors.

DYSMENORRHEA AND ARTIFICIAL MENOPAUSE

To the Editor:—A woman aged 36, married twelve years, with no children (she has never used contraceptives), has always had severe menstrual pain. In fact, no medication ever gave relief until about one year ago, when I started giving pantopon hypodermically. This seemed justified in view of the excruciating pain and of the fact that it is given only once a month. The effectiveness of pantopon is still as great as a year ago and she does not suffer nearly as much. Now this patient wants my opinion as to x-ray treatments for a therapeutic menopause. She argues that the chances of her having children are slight at this age after twelve years of sterility and that her life from now till the natural menopause would certainly be much happier without the dreaded periods. Would the symptoms of the menopause induced by irradiation differ at all from the symptoms of a natural menopause? Is the effect on sexual desire any different? I have studied this particular case for several years and have tried everything recommended for dysmenorrhea, including progesterone, chorionic gonadotropin and even a dilation and curettement, which was recommended by a gynecologist in consultation. All these were ineffectual. So I am anxious for an opinion on the effect of x-ray treatments.

M.D., New York.

ANSWER:—The symptoms of the menopause induced by roentgen or radium therapy are similar to and ordinarily not notably more severe than those of the natural menopause. There is persistence of satisfactory libido in nearly one half of the cases, although some decreased desire is to be anticipated.

In a case such as this, at the age of 36, most gynecologists would advise strongly against induction of an artificial menopause. An abdominal operation with removal of the menstruating portion of the uterus or resection of the presacral nerve would be the procedure of choice, provided palliative measures fail to bring comfort.

The following dysmenorrhea regimen merits a trial: Beginning three days before the expected onset of pain or menstruation, the patient should be outdoors as much as possible, be on a sparing diet, keep the bowels free and take 1 teaspoon of elixir of phenobarbital three times daily. With onset of pain or menstruation the patient should rest quietly, double the dosage of elixir of phenobarbital and take one-half grain (0.03 Gm.) of codeine sulfate every half hour until relief, not in excess of six tablets in twenty-four hours.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in *THE JOURNAL*, December 21, page 2203.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, February 10-12. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral*. Part II, Cleveland, May 31-June 1. Final date for filing application is April 1. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Parts 1-A and 1-B, Feb. 17. Final date for filing application is Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Part II, Groups A and B, Cleveland, May 28-June 1. Final date for filing application is March 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral*. Cleveland, May or June. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written*. Cleveland, June 1-2. Final date for filing application is May 1. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, March 30-31, following the Region I meeting of the American Academy of Pediatrics. Chicago, May 18, following the Region III meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY: *Oral*. Cleveland, May 30-June 1. Final date for filing application is April 15. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

Rhode Island July Report

Dr. Robert M. Lord, secretary, Division of Examiners, reports the oral and written examination for medical licensure held at Providence, July 11-12, 1940. The examination covered 8 subjects and included 75 questions. An average of 80 per cent was required to pass. Nine candidates were examined, all of whom passed. One physician was licensed to practice medicine by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1938)		83
Johns Hopkins University School of Medicine.....	(1920)		83
St. Louis University School of Medicine.....	(1939)		89.5
Hahnemann Medical College and Hospital of Philadelphia.....	(1939)	80, 85, 85, 88	
McGill University Faculty of Medicine.....	(1938)		86
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin.....	(1937)		88.2
School	LICENSED BY ENDORSEMENT	Year Endorsement Grad.	of
Boston University School of Medicine.....	(1938)	N. B. M. Ex.	

California June Report

Dr. Charles B. Pinkham, secretary, California State Board of Medical Examiners, reports the written examination for medical licensure held at San Francisco, June 25-27, 1940. The examination covered 9 subjects and included 90 questions. An average of 75 per cent was required to pass. One hundred and sixty-three candidates were examined, 155 of whom passed and 8 failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists.....	(1940)	77.2, 79.1, 80.9, 84	
Stanford University School of Medicine.....	(1939)		85.3,
(1940)	76.2, 76.4, 76.7, 77.6, 79.3, 79.4, 79.8, 80, 80.1,		
80.3, 80.6, 81.2, 81.2, 81.8, 81.8, 82, 82.3, 82.7, 82.8,			
83.3, 83.8, 84.2, 84.2, 84.3, 84.8, 85.2, 85.3, 85.7, 85.8,			
85.9, 86, 86.1, 86.2, 86.3, 86.6, 86.8, 86.9, 87.4, 87.7,			
88.1, 88.2, 89.8, 91.2, 92.1			
University of California Medical School.....	(1940)		75.7,
75.9, 77.7, 79.1, 79.8, 80.1, 80.7, 81.8, 82.1, 82.2, 82.2,			
82.3, 82.6, 82.6, 83, 83.1, 83.9, 84.3, 84.3, 84.3, 84.4,			
84.6, 84.6, 85, 85.1, 85.1, 85.4, 85.4, 85.4, 85.6, 85.6,			
85.7, 86.3, 86.4, 86.4, 86.4, 86.7, 87.2, 87.9, 88.2, 88.3,			
88.8, 90.1, 90.2, 91.6			
University of Southern California School of Medicine..	(1940)		77.7,
81.7, 85.4, 85.7, 86.3, 90.3			
Loyola University School of Medicine.....	(1940)		85.7
Northwestern University Medical School.....	(1940)		83,
86.1, 88.9, 89.1, 89.2			
Rush Medical College.....	(1938)		82.9

University of Illinois College of Medicine.....	(1940)	79.1
University of Louisville School of Medicine.....	(1940)	88.4
Louisiana State University School of Medicine.....	(1940)	83.6
Johns Hopkins University School of Medicine.....	(1936)	80.4,
(1937)	80.7	
St. Louis University School of Medicine.....	(1940)	75.3, 77.1,
79.4, 79.7		
Creighton University School of Medicine.....	(1938)	81.4,
(1939)	76.3, 77.3, 78.7, 78.7, 84.6	
University of Nebraska College of Medicine.....	(1939)	78
Columbia University College of Physicians and Surgeons	(1940)	81.3, 82.2, 88.1, 88.8
Cornell University Medical College.....	(1939)	80.4
University of Oregon Medical School.....	(1939)	80.4
Hahnemann Med. College and Hospital of Philadelphia	(1939)	75.6
University of Pennsylvania School of Medicine.....	(1939)	78.1
Marquette University School of Medicine.....	(1940)	83.1, 84.3
University of Wisconsin Medical School.....	(1939)	79.6
Queen's University Faculty of Medicine.....	(1938)	76.1
University of Toronto Faculty of Medicine.....	(1935)	87.4
McGill University Faculty of Medicine.....	(1936)	77, 77.4, 84.3,
(1937)	84, (1939) 83.7, (1940) 79, 87.7	
Medizinische Fakultät der Universität Wien.....	(1913)	77.9,
(1937)	79.7, 86.7	
University of Oxford School of Medicine.....	(1930)	87.2
Christian-Albrechts-Universität Medizinische Fakultät, Kiel	(1911)	78
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1929)	75.6, (1932)
Hamburgische Universität Medizinische Fakultät.....	(1923)	75.9
Ludwig-Maximilians-Universität Medizinische Fakultät, München	(1908)	76.1
Thüringische Landesuniversität Medizinische Fakultät, Jena	(1921)	76.1
Universität Heidelberg Medizinische Fakultät.....	(1911)	99.4
Regia Università degli Studi di Firenze. Facoltà di Medicina e Chirurgia	(1912)	82.9

School	FAILED	Year Grad.	Number Failed
University of California Medical School.....	(1939)		1
Chicago Medical School.....	(1928)		1
Rush Medical College.....	(1938),	(1939)	2
University of Minnesota Medical School.....	(1940)		1
University of Cincinnati College of Medicine.....	(1940)		1
Marquette University School of Medicine.....	(1940)		1
McGill University Faculty of Medicine.....	(1940)		1

Book Notices

The Diagnosis and Treatment of Cardiovascular Disease. Edited by William D. Stroud, B.S., M.D., F.A.C.P., Professor of Cardiology, University of Pennsylvania Graduate School of Medicine, Philadelphia. Volumes I and II. Fabrikoid. Price, \$18, per set. Pp. 801; 1001-1825, with illustrations. Philadelphia: F. A. Davis Company, 1940.

This is a monumental contribution to the field of diseases of the heart and blood vessels. It covers the modern point of view fully. This is important, since the subject has undergone considerable change in the past two decades as regards (1) the aspects of cardiovascular fields emphasized, (2) the substitution of the functional for the purely morphologic point of view. These changes are clearly reflected in this treatise. The sixty-two chapters of this two volume textbook are contributed by fifty-six eminent American authorities, the majority of whom have themselves advanced the knowledge of the subdivision about which they write. Being, almost without exception, clinicians as well as investigators, they write from the practical side based on experience in handling patients. They have thus presented the practical information for diagnosis and therapy in addition to the general concepts of diseases of the heart and blood vessels. The influence of the American Heart Association, in which many of the authors have taken a leading part, is evident throughout the book, and it is crystallized in the chapter on the public health aspects of heart disease contributed by Marvin.

An idea of the scope of the volume can best be appraised by an enumeration of the various contributions (space does not permit much more in this review).

The introduction, written by Sprague and P. D. White, orients the reader with regard to the prevailing emphasis of the various aspects of the subject. Maude Abbott presents a brilliant summary of congenital anomalies. Rheumatic heart disease is covered in three chapters contributed by McEwen, Paul and Duckett Jones. Bacterial endocarditis is reviewed by William Dock; cardiovascular syphilis is covered in two chapters by Paullin and Minnick and by Stokes and Anderson. L. A. Conner reviews the subject of cardiac neuroses, Porter the effects of anemia and Durant that of pulmonary diseases. The interrelation of the kidneys and the cardiovascular system is beautifully

handled by Hayman. Barr has summarized the relationship of diseases of the endocrine system and the circulation, and Thomas the relationship of hyperthyroid activity and the heart. Soma Weiss presents an excellent review of the effects of nutritional deficiency diseases on the heart. Barber contributes the chapter on trauma, Porter and P. D. White the chapters on pericarditis, Roesler the one on cardiac enlargement, Vander Veer the one on chronic valvular heart disease and Fred Smith, Robert Lévy and Stroud the three chapters on coronary artery disease and angina pectoris. Bellet summarizes the subject of the blood supply of the heart, King the normal heart, Wolferth and Margolies the subject of heart sounds, Wilson, and Bellet and McMillan the field of electrocardiography, Margolies the field of roentgenography, Herrmann the subject of cardiac arrhythmia, and Bromer and Stroud the conditions of congestive heart failure and left heart failure (and paroxysmal cardiac dyspnea).

The general management of the cardiac patient is dealt with separately by several contributions: on digitalis by Stroud and Vander Veer, and by McMillan and Bellet, on quinidine by Kerr, on physical and spa therapy by Comstock and Stroud, and on rehabilitation in industry by Stroud. Surgery and pregnancy in the cardiac patient are amply discussed by Levine. The surgical treatment of heart disorders is reviewed by Beck, with special chapters on alcohol nerve block in angina pectoris by Grant and on total thyroidectomy by Blumgart and Riseman.

The subject of peripheral vascular diseases is begun by a consideration of normal blood pressure by E. V. Allen, of capillary circulation by DeGraff and Kossman, and of venous pressure by Schleiter. Shock is presented by Freeman, hypertension by Stieglitz and by Houston, low arterial pressure by J. H. Barach, arteriosclerosis by Eli Moschowitz, periarteritis nodosa by Farley, thrombo-angiitis obliterans by Buerger, erythromelalgia, lymphedema and sudden vascular occlusion by E. V. Allen, thrombophlebitis by N. W. Barker, aneurysm and auriculoventricular fistula by Hines, arteriosclerosis obliterans, acrocyanosis and Raynaud's syndrome by I. S. Wright, and vascular anomalies and varicose veins by de Takats. An excellent article on edema by Landis concludes the book.

From the foregoing outline it is obvious that some reduplication is unavoidable, but the extent of reduplication present in this book could have been considerably curtailed by judicious editorial deletions, and this would have improved the treatise and considerably abbreviated it. The fault inherent in any volume contributed by many authors is that the style is variable, and this is true in the present work. It is, however, unavoidable. There is the advantage of range of appeal, which satisfies various readers. Readers ranging from the medical student to the specialist in cardiovascular diseases will find much in this book which will interest them. The profuse use of illustrations, case reports, selected bibliographies and an excellent index enhance the value of the book. It is regrettable that in the final proofing the fact was overlooked that a few of the illustrations were upside down and that singular instead of plural reference to their own opinion was used in one of the chapters by the joint authors. By virtue of the division of topics discussed, some topics, for example myxedema heart, have been omitted. Considerable improvement might also have been attained in the book by a better arrangement of the sequence of the chapters and by subdividing it into major sections. The innovation of showing engravings and short biographies of the men who have made the milestones in cardiovascular diseases is appealing, especially since the engravings themselves are so excellently executed.

This treatise is a splendid cooperative effort and it should be in the library of every one who is interested in the subject of cardiovascular diseases. The reviewer can recommend the book no better than Sir Thomas Lewis, who in the foreword states: "The brilliant list of American authors of the present contents includes a score of names known in every part of the world where cardiovascular diseases have been intensively studied; they are known for the solid contribution of those who bear them to their subject. Rarely before has such a number of authoritative writers combined to place its views of a branch of medicine on record, and never before of cardiovascular disease; it is a guaranty to the reader that he is in direct or close contact with all the fountains of modern knowledge, the most important guaranty perhaps that any reader can be given."

Der Klinische Blick. Von Prof. Dr. Erwin Risak. Third edition. Paper. Price, 6.60 marks. Pp. 230. Vienna: Julius Springer, 1940.

Dr. Risak presents no new or startling discoveries. He merely presents a careful survey of objective clinical phenomena that are readily observable when the physician makes use of his five senses. He leads the reader on to the interpretation and coordination of these observations, proceeds to the development of what should be the birthright of every true clinician, namely insight or what is at times called clinical intuition, the ability rapidly to evaluate the importance of seemingly widely different phenomena, and to fit them into the harmonious picture of clinical syndrome or disease entity. A pupil of the school of von Hochenegg and Chvostek, and remotely of Bamberger, Skoda and Auenbrugger, Dr. Risak comes to this approach quite naturally and his contribution is useful. Particularly in this day when medicine in Europe must be practiced in mass, the capable clinician must have the ability to sort his material rapidly but surely. It is here that clinical insight, the "clinical eye," is of utmost value. Risak would by no means have the accessory laboratory aids or the use of the modern diagnostic armamentarium neglected, but he is quite right in stressing the significance of the art of medicine as an important though often neglected phase in our modern medical training. The book is well ordered. The first part concerns the physician, the second part the environment of the patient, and the third part, of approximately 150 pages, the phenomena to be observed in the patient. The presentation is both thorough and instructive but sufficiently informal and personal to be entertaining as well. Shrewd clinical observations illustrate and enliven the significant points, all of which have been selected from a practical point of view. It is to be regretted that nothing quite comparable to this little volume has appeared in the more recent American literature.

A Pioneer Doctor in Old Japan: The Story of John C. Berry, M.D. By Katherine Fiske Berry. Cloth. Price, \$2.50. Pp. 247, with 21 illustrations. New York, London & Edinburgh: Fleming H. Revell Company, 1940.

Dr. John Cutting Berry went to Japan in 1872 when he was 25 years old. He was the type of medical missionary who has done probably more for good will between Eastern and Western civilization than has any other pursuit. The Japanese published in their own language a short biography of his life, the first ever written about an American by the Japanese. Dr. Berry was decorated by the Japanese emperor and was hailed by the Japanese as the father of prison reform and social service work in their country. At the time of the celebration of the golden wedding of Dr. Berry the Japanese presented him with a marvelous Japanese vase; there were messages from innumerable Japanese leaders.

In the course of his medical education Dr. Berry studied under W. W. Keen and S. Weir Mitchell. He took also some lectures under Oliver Wendell Holmes. The writer has a fine sense of humor and intersperses her story with innumerable anecdotes. There are excellent pictures of Japanese civilization.

After leaving Japan in 1894 Dr. Berry settled in Worcester, Mass., as a specialist in diseases of the eye, ear, nose and throat. He practiced medicine until his eighty-eighth year. In 1918 he was appointed head of an American board to survey conditions in Japan. Thus he lived a long and useful life which was well worthy of the sympathetic record now available in this book.

Mucous Colitis: A Psychological Medical Study of Sixty Cases. By Benjamin V. White, M.D., Stanley Cobb, M.D., and Chester M. Jones, M.D. Psychosomatic Medicine Monograph I. Published with the Sponsorship of the Committee on Problems of Neurotic Behavior, Division of Anthropology and Psychology. Paper. Price, \$2. Pp. 103, with 30 illustrations. Washington, D. C.: National Research Council, 1939.

For years many gastro-enterologists have felt that the term "mucous colitis" is undesirable because in this disease the colon itself is normal and the distress is due only to nervous stimuli arising in a tired or psychopathic brain. Under the circumstances it seems unfortunate that the writers of this valuable little monograph decided to retain the term "colitis." Since the genitive ending *itis*, which meant originally "disease of a part," has come to mean in both the popular and the medical mind "inflammation," it seems wrong to use it in describing a disease in which the organ involved is not inflamed or ulcerated. The use of the term is particularly unfortunate when there is such a disease as true ulcerative colitis and patients are constantly

being confused. They get the idea that they have a serious and fatal disease and naturally become frightened. The remarkable contribution of White, Cobb and Jones is the demonstration now that, by injecting into healthy students a drug of the acetylcholine type which produces reactions similar to those of stimulation of the parasympathetic nerves, one can produce changes in the mucosa of the bowel which somewhat resemble those seen during an attack of mucous colic. Every gastro-enterologist will want to have a copy of this monograph within reach of his desk.

Berkeley Moynihan, Surgeon. By Donald Bateman. With a preface by Lord Moynihan. Cloth. Price, \$4. Pp. 354, with 8 illustrations. New York: Macmillan Company, 1940.

Unquestionably during his career Berkeley Moynihan was the most famed of all British surgeons. He was a frequent visitor to the United States and was the personal friend of many a great American surgeon. His biography has now been made available by Dr. Donald Bateman, who traces the life of the famous surgeon, describing his birth and his parenthood. Berkeley Moynihan derived many of his characteristics from a remarkable father and mother. Then came the decision as to whether or not the boy at the age of 15 would be developed for a military career or a career in medicine. He made his own choice and entered medical school in 1883. He had a retentive memory and great strength. He had planned after he entered medicine to join the army medical service but he came to the attention of the surgeon McGill and became a dresser. After graduation he was, however, appointed to become house surgeon for Mayo-Robson. Then comes an intimate account of the life of Moynihan as a young doctor and of his marriage. In 1914 the outbreak of the great war interrupted his work but gave him opportunity for fame. His first visit to the United States was in 1903, at which time he spoke at the College of Physicians of Philadelphia, discussing a paper by Dr. William J. Mayo on "Surgery of the Stomach and Duodenum." Following his return from America he introduced the use of rubber gloves and of the white coat into his surgery. It is interesting to read that because of this he was the subject of much ridicule. In the course of his development he practiced constantly the tying of knots and developed his manual skill. At the age of 40 he found himself being occasionally invited to speak in public and he soon developed a gift for witty and felicitous oratory. This accomplishment also played a great part in his advancement both in science and in public life. In July 1917 he again visited the United States in connection with our preparation for entrance into the World War. This volume makes available some of the best paragraphs from the many addresses which he made at that time in America and also provides some of his letters to his wife which discuss those travels. These are among the most interesting and valuable contributions in the book. The volume continues to trace the career of the great surgeon to the time of his death and affords many interesting sidelights on his career. It is readable and inspiring, picturing the great surgeon more as a man than as a scientist. It may well be added to the number of inspiring biographies now available in the field of medicine. If there is any criticism of the work, it is the absence of an index.

Sex in Development: A Study of the Growth and Development of the Emotional and Sexual Aspects of Personality Together with Physiological, Anatomical, and Medical Information on a Group of 153 Normal Women and 142 Female Psychiatric Patients. By Carney Landis et al. With a foreword by Nolan D. C. Lewis. Cloth. Price, \$3.75. Pp. 329. New York & London: Paul B. Hoeber, Inc., 1940.

Here is the report of a research carried out under the auspices of a special committee of the National Research Council. Some 295 women were interviewed as to their sex life. They had physical and gynecologic examinations, and a number of experts in the field of sex study took part in an analysis of the results. It was, of course, impossible to submit each one of these women to a psychoanalysis. The method was instead the study and tabulation of material from medical and psychiatric case histories and reports. Each person interviewed was presented with a series of cards. Each card contained a single question. The answers were recorded verbatim. Next came an interview with questions concerning the facts and fantasies related to psychosexual development. The interview was supplemented by two questionnaires, one dealing with vocational interest and the other

with a marriage inventory. Then came physical examination, roentgenologic studies of the pelvis and a psychiatric case history. The work is divided into chapters dealing with adolescence, adult sex practices, marriage adjustments, course of development, psychiatric studies of normal women, homo-erotic women, unhappily married women and psychopathologic personalities.

The evidence developed indicates that psychosexuality has its origins long before puberty. The way in which sex knowledge is gained seems to affect later attitudes. The child who has many illnesses or who is continually sick frequently exhibits difficulties in personal adjustment in adult life. The most important problem which a girl faces in adolescence is that of freeing herself from family ties. The onset of menstruation does not seem to have any radical effects in personality formation. Masturbation is a common practice which usually disappears without untoward effects on the personality. One woman in every four interviewed had sexual intercourse before marriage, with a higher percentage among girls with native born parents than among girls with foreign born parents. Apparently the determination of sexual intercourse before marriage depends in part on the standards of the social group to which she belongs, her psychology and her physical attractiveness. The evidence showed that one wife out of every three is sexually maladjusted. These and many other facts became apparent from the psychologic aspects of this study. From a physical point of view there were surprisingly few anatomic or physiologic differences between normal woman and those who suffered from functional or mental disturbances. Tendencies toward the male body form were found associated with homo-eroticism. The chief finding was the observation that the neurotic personality represents a style of life which is consistent from an early age. The volume is supplemented with samples of the examination forms that were used, tabular data, an extensive bibliography and a good index.

The International Medical Annual: A Year Book of Treatment and Practitioner's Index. Edited by H. Letheby Tidy, M.A., M.D., F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc. Fifty-Eighth Year, 1940. Cloth. Price, \$6. Pp. 545, with 127 illustrations. Baltimore: William Wood & Company, 1940.

This work is now in its fifty-eighth year. It is a compilation of contributions by a considerable number of British physicians who, through a system of abstracts of recent medical literature, keep knowledge up to date. The book is compiled on an alphabetical basis. It is freely illustrated and has an adequate index for ready reference. As a compilation of the literature of the previous year, with particular reference to the British point of view, it may be unhesitatingly recommended.

Tratado de enfermedades nerviosas. Por Luis Barraquer Ferré, Ignacio de Gispert Cruz y Emilio Castañer Vendrell, jefe y auxiliares respectivamente del Departamento de neurología del Hospital de la Santa Cruz y San Pablo de Barcelona. Tomos I y II. Cloth. Pp. 1,154, with 448 illustrations; 1,108, with 396 illustrations. Barcelona & Buenos Aires: Salvat Editores, S. A., 1936, 1940.

These two large volumes are said to be based mainly on the clinic and teachings of Dr. L. Barraquer Roviralta of the Hospital de la Santa Cruz y San Pablo de Barcelona, to whom it is dedicated. The preface by Pierre Marie is worthy of Mark Twain. After a brief historical sketch which is hardly more than a list of names the authors begin with a discussion of the methods of examination, which is adequate although physiologic observations are interspersed in a manner more confusing than illuminating. This section covers 270 pages.

The treatise proper begins with a section on the peripheral somatic nerves, which is good; the discussions are brief and generally accurate and there is an excellent description of the polyneuritis of leprosy. Nothing is said of the possibility that avitaminosis may play a role in the causation of alcoholic polyneuritis. The authors state that paralysis of the glossopharyngeal nerve causes dysphagia, a statement not confirmed by the results of surgical section of that nerve. Experience gained in the Spanish war is clearly reflected in the discussion on wounds of the nerves of the extremities. The brief remarks concerning tumors of the peripheral nerves are inadequate. Proper advice is given concerning the surgical treatment of various neuralgias.

The second and much longer section of the treatise concerning diseases of the spinal cord begins with a brief and unrelated sketch of the histology and histopathology of the central nervous

system. Then follows a short discussion of the anatomy and physiology of the spinal cord, after which the various diseases follow in encyclopedic fashion, each one being discussed in all its phases, including pathology. One notes an unusual chapter on echinococcus in the spinal canal. The second volume begins with 197 pages on the sympathetic nervous system in which American work is quoted at second hand if at all. Then follows a chapter on disorders of the extrapyramidal system, as though they had nothing to do with the brain.

The third section of the treatise deals with the diseases of the brain; extrapyramidal diseases such as Parkinson's disease and Wilson's disease were dealt with before. The discussions of cerebral diseases follow the same lines as do those of the spinal cord; after an anatomic introduction and short chapters on aphasia and apraxia the various diseases are taken up one by one and discussed from every point of view. The discussion of brain tumors occupies 140 pages and again one has the impression that American work is quoted at second hand (no bibliography is appended to this treatise).

The work is well illustrated with many interesting original photographs. One gains the impression that the authors are thoroughly familiar only with French neurology. Recent medical advances, such as quinine for myotonia congenita or potassium for periodic family paralysis, are not mentioned. The work is a compilation, doubtless useful in Spain; but the North American neurologist, with Wilson's masterpiece at his disposal, will rarely find need to consult it.

The Art of Useful Writing. By Walter B. Pitkin, Professor in Journalism, Columbia University, New York. Cloth. Price, \$2. Pp., 261, with illustrations. New York & London: Whittlesey House, McGraw-Hill Book Company, Inc., 1940.

Professor Pitkin has been author, dean and teacher and has previously written books on the art of rapid reading and on the art of learning. He recommends that the way to learn to write usefully is first to learn to write much. He recommends particularly study of condensation. In his own practice he learned eventually to write 1,500 words an hour and he now claims that he can write 10,000 words in finished book copy in nine consecutive hours. He recommends also that every writer plan to organize his information in useful files. His book is full of useful information but whether or not it is possible by the use of a book of this kind to become a writer one can only say that Mr. Pitkin says that it is. He provides innumerable exercises and plans for study. No doubt any one who has a talent and an urge for writing will be helped by this book. As an old practitioner in the writing field, the reviewer is inclined to believe that without this urge and talent any amount of sweat and exercise will not produce writing that is useful or salable.

Die Entzündungsbestrahlung. Von Dr. med. habil. R. Glauner, Dozent für Röntgenologie an der Universität Köln. Boards. Price, 15 marks. Pp. 190, with 14 illustrations. Leipzig: Georg Thieme, 1940.

Illustrative of the enlarging field for application of roentgen therapy other than in the treatment of cancer, this book is a welcome addition to the literature, constituting an excellent summary of the known technical and clinical facts relative to the subject. After a brief historical introduction and a discussion of the concept of inflammation, the author proceeds to the full consideration of the effect of the roentgen rays on local inflammatory processes from the standpoint of the physical and chemical changes, the blood vessels, the exudates, the mesenchyma and ferments. Next comes the discussion of the influence of the roentgen rays on the exciting causes of inflammation and on the general defensive mechanism of the organism against inflammation, including the antibactericidal blood and serum reactions, the reticulo-endothelial systems, the action of the protein bodies, the blood picture and the vegetative nervous system. The clinical subsidence of experimental inflammation under roentgen irradiation is next studied from the standpoint of bacterial, mechanical and chemical inflammation. Then the author proceeds to a general clinical consideration of anti-inflammatory irradiation, giving the indications and contraindications, general technic and dosage. The second part of the book is devoted to a discussion of radiation therapy in inflammations by systems, including a long list of inflammatory lesions in which the value of roentgen therapy is but slightly appreciated by the majority of the medical profession. This book, which is

gotten up in such an authoritative manner, should serve to stimulate a much wider use of roentgen therapy in the treatment of inflammations.

Three Famous Occultists. Dr. John Dee. By G. M. Hort. Franz Anton Mesmer. By R. B. Ince. Thomas Lake Harris. By W. P. Swainson. Cloth. Price, \$2. Pp. 190. Philadelphia: David McKay Company, [n. d.].

In the sixteenth century John Dee practiced as an astrologer. In those days the drawing of horoscopes was considered a science. Dee actually drew horoscopes for Queen Mary and for her sister Princess Elizabeth. Among other contributions he wrote a work on naval defense. Early in his career he became interested in psychic manifestations, recording his dreams and other phenomena. He also is credited with having practiced crystal gazing and the original crystal is still available in the British Museum.

Franz Anton Mesmer has been the subject of many biographies. He was the originator of magnetic healing, constantly in debate with the medical faculty of his time. In 1784 a commission was appointed to investigate the claims of animal magnetism and published a report which refuted his claims. At that time the scientific study of suggestion was not yet known. A description of his technic indicates that the results were secured by the power of suggestion, which was enhanced by the laying on of hands and by some complicated apparatus.

The third of the occultists, Thomas Lake Harris, was an Englishman who came early to America. In 1844 he was a Universalist preacher in New York. He became an occultist in 1850, when he first experienced what he termed "internal respiration." As was customary in those days, he formed a community to be called the Brotherhood of the New Life, which practiced occultism in a form which was apparently a mixture of astrology, alchemy and other esoteric manifestations. He had a system of religious philosophy based on christianity, and he claimed to have overcome death. When he himself died, many of his followers lost interest.

Government and Economic Life: Development and Current Issues of American Public Policy. Volume II. By Leverett S. Lyon and Victor Abramson. With the collaboration of Charles L. Dearing, et al. The Institute of Economics of The Brookings Institution Publication No. 83. Cloth. Price, \$3.50. Pp. 1,301. Washington, D. C.: Brookings Institution, 1940.

This is the second volume of a series on American public policy in relationship to economic life prepared through the Brookings Institution and published by it. In this volume the major portion of the discussion concerns government and the special treatment of private enterprise. One chapter deals with the activities of the government in the field of foods and drugs. There are also chapters on public relief and on social security. In their concluding observations the authors incline to the view that "our economy has reached a stage which is denominated as 'mature' and that as a result there is no longer any hope that we shall be able to come near the full employment of our productive resources without a continuous program of extensive public spending designed specifically to promote the utilization of idle men and plant." They recognize that it has not been demonstrated by economic analysis or by practice that the means now in operation for meeting the problem of unemployment will do more to meet the situation than the less elaborate programs of the early thirties. They say, however, that a permanent program of extensive governmental spending raised great questions of effectiveness and perhaps the survival of private enterprise.

A Surgeon Explains to the Layman. By M. Benmosché, M.D. Cloth. Price, \$3. Pp. 317, with diagrams by Bhola D. Panth. New York: Simon & Schuster, 1940.

While there are innumerable works of medicine planned primarily for the public, no one has previously attempted to inform the lay reader concerning all the technical details and background of surgical procedures. To this extent Dr. Benmosché is a pioneer. The information is for the most part sound and readable. He does not attempt to cover the history of surgery as in Graham's excellent book "The Story of Surgery." If any one wants to know about his operation before he has it, there is probably no better guide. However, from the point of view of the patient there may be some question as to the desira-

bility of a work of this character. In every instance the reader is made to feel that the decision of when to operate or whether or not to operate at all is an exceedingly difficult one. Incidentally it is a task which the surgeons find sufficiently difficult without having to enter into debate with the uninformed patient. Of chief value in the work are the simple discussions of the anatomy of various portions of the body. Particularly impressive are the final discussions of surgery of the chest, the brain and the heart. Quite recently the picture periodicals have illustrated every step of several surgical operations and there has been at least one broadcast directly from an operating room. Thus a beginning has been made. It will be interesting to observe the ultimate effect of information for the public concerning the technical details of operative procedures.

Electric Light for the Farmstead. Prepared by Bureau of Agricultural Chemistry and Engineering and Home Economics. U. S. Department of Agriculture, Farmers' Bulletin No. 1838. Paper. Price, 10 cents. Pp. 61, with 43 illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1940.

This bulletin stresses the importance of good lighting and discusses in detail the essentials for good lighting. Further, it describes methods for providing good light for the farmhouse. The types of electric outlets, remodeling old lighting installations and equipment as well as lighting the farm yard and lighting the farm buildings are discussed. Information on planning lighting for farm buildings is given and is based on observations and records of the Department of Agriculture.

Pharmacology and Therapeutics. By Arthur R. Cushny, M.A., M.D., LL.D. Twelfth edition revised by C. W. Edmunds, A.B., M.D., Professor of Materia Medica and Therapeutics in the University of Michigan, Ann Arbor, and J. A. Gunn, M.A., M.D., D.Sc., Professor of Pharmacology and Director of the Nuffield Institute for Medical Research, University of Oxford, Oxford. Cloth. Price, \$6.50. Pp. 852, with 66 illustrations. Philadelphia: Lea & Febiger, 1940.

Since its first appearance in 1899 this work has been enjoying increasing popularity in Great Britain and the United States as a standard textbook and as a reference book on the subject of pharmacology by teachers, students and practitioners. Considerable revision has been made in the twelfth edition, beginning with the title, which was formerly "A Text-Book of Pharmacology and Therapeutics, or the Action of Drugs in Health and Disease" but now bears the simplified wording "Pharmacology and Therapeutics," extending through the introduction, the subject material and the index. Some of the changes are minor in nature but many involve considerable revision and even the addition of subjects formerly foreign to this book. Hardly a section has escaped some revision, but included in the sections which have undergone major changes, rewriting or additions are those describing the heavy metals and metalloids, alcohol-chloroform group, soporifics or hypnotics, local anesthetics, nicotine group, drugs of internal secretion and the vitamins. Several totally new descriptions have been inserted, including pharmacologic syndromes in the introduction, benzedrine, sex hormones, sulfanilamide, sulfapyridine and allied compounds and mandelic acid. These additions account for most of the increase in size of forty-four pages.

The section on the opium series remains as excellent as ever and includes a new member, bulbocapnine, an alkaloid closely related to apomorphine. One of the most useful and unique features in Cushny's Pharmacology and Therapeutics has been the classification of drugs according to their therapeutic uses. The student has always appreciated this section.

It is difficult to prepare a textbook on pharmacology for two countries such as Great Britain and the United States of America, as there is considerable difference in the nomenclature. For example, butyl-bromallyl barbituric acid is known as pernoc-ton in England and this is the name which appears in the text. In the United States the preparation is known as pernoston. Another example is seen under the section on avertin. In the British market avertin is supplied as avertin fluid but on the American market it is supplied as avertin with amylene hydrate, the amylene hydrate possessing anesthetic properties almost equal to those of avertin. However, even with such differences the subject material is so clearly and interestingly written that even the student will encounter few difficulties in his reading.

Although the index has been enlarged, it still appears to be too conservative for a book which contains so much information.

Unfortunately, the publishers have changed the color of the cover from the former familiar green to a red which is not unlike the covers of other well known books on pharmacology. No longer can one go to the library and easily pick out this book by its distinctive color. However, it will still remain one of the most popular works on pharmacology.

A Manual of the Common Contagious Diseases. By Phillip Moen Stimson, A.B., M.D., Assistant Professor of Clinical Pediatrics, Cornell University Medical College, New York. Third edition. Fabrikoid. Price, \$4. Pp. 465, with 60 illustrations. Philadelphia: Lea & Febiger, 1940.

Complete revision of a previously excellent textbook on the contagious diseases has produced here a book of great value. The subjects discussed include the principles of contagion, serum reactions, detailed description of the common contagious diseases, general management of these disorders, and management in boarding schools and homes. The material is presented briefly and the appended references increase the value of the work. Included is a discussion of the use of sulfanilamide and sulfapyridine. The book covers practically every phase of the subject without wordiness, so that physicians, students and nurses will find satisfaction in having this volume at their disposal.

Behind the Surgeon's Mask. By James Harpole, pseud. Cloth. Price, \$2.75. Pp. 308. New York: Frederick A. Stokes Company, 1940.

Here is another collection of interesting anecdotes from the practice of medicine by a British writer who has exceptional qualities in the field of letters. He has, moreover, an excellent sense of the dramatic and is able to make fascinating the incidents which many another physician might pass as commonplace. Both doctors and layman will find this book interesting. Moreover, it has none of the aspects of horror or tribulation which make many such works forbidden for the invalid.

A Survey of the Hospital Dietitian and Her Job. Parts I and II. By S. Margaret Gillam, Department of Nutrition, The New York Hospital, New York. Reprinted from Journal of the American Dietetic Association Vol. XVI: Nos. 6 and 7, 1940. Paper. Pp. 41. Chicago, 1940.

This is a report of a study of the hospital dietitian and her functions, activities and professional relationships. It is based principally on the questionnaire method.

Aids to Inorganic Chemistry. By R. G. Austin, B.Sc., A.I.C., F.R.M.S., Associate of University College, Southampton. Cloth. Price, \$1.50. Pp. 348. Baltimore: William Wood & Company, 1940.

This brief handbook provides the fundamental information regarding inorganic chemical substances that is necessary to all students in elementary courses on chemistry. The book should be especially valuable as an aid in preparation for examination.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Foot Drop Following Operation on the Knee; Res Ipsa Loquitur.—The plaintiff ruptured the exterior lateral and posterior crucial ligaments of his left knee and engaged the defendants to repair the damage. An operation was performed consisting of the removal of the damaged portions of the ligaments and the substitution of new material obtained from the fascia lata and biceps femoris muscle of the left leg. After the operation, the plaintiff began to suffer from a foot drop, and an examination by physicians other than the defendants disclosed that the peroneal nerve, the nerve supply to the muscles which raise the foot, was severed in the vicinity of the knee. The plaintiff then sued the defendants, alleging negligence, and judgments for the defendants resulted. After the case had been considered by the district court of appeal, California (80 P. (2d) 96; abstr. *J. A. M. A.* 112:1419 [April 8] 1939), the plaintiff appealed to the Supreme Court of California.

The medical testimony in this case, said the Supreme Court, showed without contradiction that, although the severance of the peroneal nerve is something which ordinarily does not occur in operations such as that performed in this case, yet even

when the precautions prescribed by the approved technic are taken, there may be a break of or an injury to the nerve in from 5 to 9 per cent of the cases. The court could find nothing startling about such evidence and was of the opinion that it afforded no basis for the recovery of damages. Probably in any operation, the court observed, there is some hazard which the medical profession recognizes and guards against but which is not always overcome. To say that the doctrine of *res ipsa loquitur* permits the recovery of damages in every case where an injury does not ordinarily occur would place a burden on the medical profession which the law has not heretofore laid on it. On the contrary, the law has never held a physician or surgeon liable for every untoward result which may occur in medical practice. It requires only that the physician shall have the degree of learning and skill ordinarily possessed by physicians of good standing practicing in the same locality and that he shall use ordinary care and diligence in applying that learning and skill to the treatment of his patients. Whether he has done so in a particular case is a question for experts and can be established only by their testimony. When the matter in issue is one within the knowledge of experts only and is not within the common knowledge of laymen, the expert evidence is conclusive. Negligence on the part of a physician will not be presumed; it must be affirmatively proved. In the absence of expert testimony it will be presumed that a physician exercised the ordinary care and skill required of him in treating his patient.

It is true, the court continued, that in a restricted class of cases the courts have applied the doctrine of *res ipsa loquitur* in malpractice cases. But it has been invoked only where a layman is able to say as a matter of common knowledge and observation that the consequences of professional treatment were not such as ordinarily would have followed if due care had been exercised. For example, it has been applied in California where a sponge was left in the body of the patient, where the patient was burned by the application of hot compresses or heating apparatus or through the operation of an x-ray machine and where the patient sustained an infection through the use of an unsterilized hypodermic needle. In each of these situations, however, the rule was applied because, in the opinion of the court, common knowledge and experience teaches that the result was one which would not have occurred if due care had been exercised. In the present case, however, an entirely different situation existed. Here what was done lies outside the realm of a layman's experience. Medical evidence is required to show not only what occurred but how and why it occurred. That evidence in the present case established beyond question, the court thought, not only that the peroneal nerve may be injured even when due care is used but that this unfortunate result invariably occurs in a limited number of cases. The doctrine of *res ipsa loquitur* is therefore entirely inapplicable and no malpractice was proved. The court, therefore, affirmed the judgments for the defendants.—*Engelking v. Carlson (Calif.)*, 88 P. (2d) 695.

Optometry: Sale of Eyeglasses by Optometrist Subject to Retail Sales Tax.—In two decisions, one emanating from Pennsylvania and the other from California, the question of the applicability of a retail sales tax to sales of eyeglasses by optometrists was decided. In each case the optometrist, after testing his patient's eyes and prescribing glasses therefor, sent the prescription to a dispensing optician, received the glasses therefrom and then delivered them to the patient. The bill that the optometrist subsequently sent to the patient included a fee for his professional services and a profit from the sale of the eyeglasses.

In *Kamp v. Johnson*, the plaintiff, an optometrist, sued the treasurer of the state of California to recover the amount of a tax which the optometrist had paid under protest. He contended that he was not subject to the provisions of the California Retail Sales Tax Act of 1933 because he was engaged in the practice of a profession and the furnishing of eyeglasses was purely incidental to the rendering of professional services. From an adverse judgment the optometrist appealed to the Supreme Court of California. In affirming that judgment, the Supreme Court held that the fact that the plaintiff practiced a profession was

immaterial because all the elements determinative of liability under the Retail Sales Act were present, i. e., a retail sale of tangible personal property for use by the patient and not a sale for resale, a transfer of title to the patient and the payment of a consideration therefor. In the judgment of the court the tax properly fell on the optometrist, since "the tax must be paid at some time with respect to all tangible personal property sold for use or consumption."

In *Commonwealth v. Miller*, the state of Pennsylvania sued the defendant optometrist to collect a tax assessed under the Pennsylvania Mercantile License Tax Act of 1899. It was conceded that the defendant was not liable for payment of the tax with respect to any income derived from his professional services in examining and measuring the vision of the eyes, prescribing glasses and fitting them after they were made. The defendant contended, however, that he should be declared exempt from the tax as to the selling of eyeglasses because an optometrist in selling glasses is in the same position as a dentist selling bridge-work or a physician supplying medicine to his patients. From an adverse judgment the optometrist appealed to the Supreme Court of Pennsylvania. The making and selling of bridgework by a dentist, said the Supreme Court, and the supplying of medicine to patients by a physician, instances in which the state "has very correctly not attempted to collect the mercantile tax," are radically different from the selling of eyeglasses by optometrists. In the case of the dentist, said the court, the preparation of bridgework necessitates considerable professional and scientific skill, labor and design on the part of the dentist. In the case of the physician, it is quite obvious that the furnishing of medicine to a patient is an inherent part of a physician's professional services in the treatment of sickness and disease. But the optometrist in selling eyeglasses is engaged in a business not at all necessary to his profession. He does not grind the lenses nor place them in their fittings. He plays no part in making or creating the eyeglasses. The glasses are handed to him by the maker, the optician, and he makes any necessary adjustment to fit them to the patient's head, but in so doing he makes no real change in the lenses or frames as such. No skill, scientific or otherwise, of the optometrist is required, since the scientific work has already been performed by the optician in making the glasses. In the judgment of the court the sale of eyeglasses, tangible chattel, is readily separable from the essential professional service of the optometrist, and such sale properly belongs to the occupation of the optician and is not necessary to the practice of optometry. The retail optician has always been subject to the mercantile tax and the optometrist cannot invade the optician's field of business, be a vendor of merchandise, and then claim immunity from the tax merely because he is also engaged in the profession of optometry. The court held, therefore, that the defendant was subject to the tax, and so it affirmed the judgment in favor of the state.—*Kamp v. Johnson (Calif.)*, 99 P. (2d) 274; *Commonwealth v. Miller (Penn.)*, 11 A. (2d) 141.

Society Proceedings

COMING MEETINGS

- American Orthopsychiatric Association, New York, Feb. 20-22. Dr. Norville C. La Mar, 149 East 73d Street, New York, Secretary.
- Annual Congress on Industrial Health, Chicago, Jan. 13-15. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago, Secretary.
- Annual Congress on Medical Education and Licensure, Chicago, Feb. 17-18. Dr. W. D. Cutter, 535 North Dearborn St., Chicago, Secretary.
- Eastern Section, American Laryngological, Rhinological and Otolological Society, Philadelphia, Jan. 10. Dr. N. S. Weinberger, Robert Packer Hospital, Sayre, Pa., Chairman.
- Middle Section, American Laryngological, Rhinological and Otolological Society, Chicago, Jan. 27. Dr. Walter H. Theobald, 307 North Michigan Blvd., Chicago, Chairman.
- Pacific Coast Surgical Association, Los Angeles, Feb. 19-22. Dr. H. Glenn Bell, University of California Hospital, San Francisco, Secretary.
- Southern Section, American Laryngological, Rhinological and Otolological Society, Nashville, Tenn., Jan. 8. Dr. William G. Kennon, Doctors Bldg., Nashville, Tenn., Chairman.
- Western Section, American Laryngological, Rhinological and Otolological Society, San Francisco, Feb. 1-2. Dr. Robert C. Martin, 384 Post St., San Francisco, Chairman.
- Society of Surgeons of New Jersey, Newark, Jan. 29. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia 200:577-716 (Nov.) 1940

- *Pulmonary Embolism and Heart Disease: Review of Twenty Years of Personal Experience. P. D. White, Boston.—p. 577.
- Cobra Venom: Its Use in Stenocardia: Preliminary Report. A. E. Parsonnet and A. Bernstein, Newark, N. J.—p. 581.
- Heredity in Pernicious Anemia. H. F. Stamos, Ann Arbor, Mich.—p. 586.
- Effect of Nicotinic Acid on Blood Coagulation. R. M. Calder and Grace P. Kerby, Houston, Texas.—p. 590.
- Culture of Human Marrow: Studies of Relative Effectiveness of Neosarsphenamine, Mapharsen, Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfamethylthiazole on Infections with *Streptococcus Viridans* (Alpha Hemolytic *Streptococcus*). E. E. Osgood, with technical assistance of Inez E. Brownlee and Julia Joski, Portland, Ore.—p. 596.
- Quick's Prothrombin Test Simplified by Use of Stable Thromboplastin. A. W. Souter and R. Kark, Boston.—p. 603.
- *Mechanism of Renal Hypertension. J. M. Muñoz, E. Braun-Menendez, J. C. Fasciolo and L. F. Leloir, Buenos Aires, Argentina.—p. 608.
- *Clinical Experience with Sulfamethylthiazole. A. E. Brown and W. E. Herrell, Rochester, Minn.—p. 618.
- Antipyretic Action of Sulfapyridine. P. B. Beeson and C. A. Janeway, Boston.—p. 632.
- Intubation Studies of Human Small Intestine: XV. Absorption and Expulsion of Glucose from Stomach. R. Warren, W. G. Karr, Olive D. Hoffman and W. O. Abbott, Philadelphia.—p. 639.
- Sabin Agglutination Test and Polysaccharide Skin Test (Francis) as Indexes of Recovery in Pneumonia. W. W. Fox, R. Rosi and W. L. Winters, Chicago.—p. 649.
- Diagnosis of Cause of Obstructive Jaundice by Means of Blood Picture. T. R. Waugh, Montreal.—p. 655.
- Relation of Phosphorus to Fat and Glucose Metabolism in Sprue. F. M. Hanes and R. Reiser, Durham, N. C.—p. 661.
- Central Nervous System Stimulant Effects of Dextro-Amphetamine Sulfate. M. Prinzmetal, Los Angeles, and G. A. Alles, San Francisco.—p. 665.
- Influenza Meningitis Treated with Sulfapyridine: Bilateral Ureteral Obstruction, Uremia, Recovery. J. H. Arnett, G. D. Shoup and N. W. Henry, Philadelphia.—p. 674.
- Delirium Tremens: Study of Various Methods of Treatment. M. Rosenbaum, P. Piker and H. Lederer, Cincinnati.—p. 677.
- Production of Fatty and Fibrotic Livers in Guinea Pigs and Rabbits by Seemingly Adequate Diets. M. A. Spellberg and R. W. Keeton, Chicago.—p. 688.
- *Endemic Riboflavin Deficiency in Infants and Children. T. D. Spies, W. B. Bean, R. W. Vilter, Cincinnati, and N. E. Huff, Birmingham, Ala.—p. 697.

Pulmonary Embolism and Heart Disease.—White summarizes his experience of twenty years with pulmonary embolism in association with heart disease by recounting the increasing frequency with which he has recognized the condition, the possible confusion in diagnosis, the frequency with which it complicates heart disease and the helpful signs of its presence. From 1920 to 1930 among 4,000 patients he made an initial definite diagnosis of pulmonary embolism simulating or complicating heart disease in only 9 cases and a questionable diagnosis in only 7. Among 3,350 patients in the last decade the definite diagnoses have increased from 9 to 66 and the questionable ones from 7 to 39. Of the 75 definite cases only 29 were diagnosed in the first sixteen of the twenty years, while 46 cases were encountered among 1,350 patients in the last four years. The author is certain that this increase in the last few years has not been actual but that a large part of it has been due to better recognition of the condition. Twenty-eight of the 75 definite cases simulated and 47 complicated heart disease. The cardiac diagnoses in which pulmonary embolism or infarction occurred as a complication were coronary disease, mostly with myocardial infarction and with or without hypertension, in 26; rheumatic heart disease, mostly with mitral stenosis and auricular fibrillation, in 15; hypertensive heart disease in 2, patent ductus arteriosus with subacute bacterial endocarditis in 1 and cardiac enlargement with no other evident abnormality than chronic auricular

fibrillation or flutter in 3. Peripheral phlebitis was evident in only a few cases, but it is probable that the majority might have shown such a lesion if the veins could have been explored; at least that is the lesson to be derived from the postmortem observations in which phlebitis that gives little or no clinical evidence of its presence is found in 70 per cent of cases of medical pulmonary embolism. Pulmonary embolism has failed to attract the interest and attention it has deserved from general practitioners as an important medical disease in nonsurgical and nonobstetric cases. Usually pulmonary embolism is either so mild or so rapidly fatal that characteristic electrocardiographic abnormalities are not present or the patients are examined only after the height of the effect of the pulmonary arterial obstruction has passed. Pulmonary embolism and infarction are easily overlooked, especially in the presence of congestive heart failure, when they are most common; or they are erroneously diagnosed as pneumonia, congestive heart failure or coronary thrombosis. Clues to the diagnosis lie in unexplained fever, leukocytosis, tachycardia, faintness, prostration, dyspnea or even jaundice, especially in a patient with heart disease.

Mechanism of Renal Hypertension.—Muñoz and his associates epitomize the present knowledge of the mechanism of renal hypertension as follows: Renal ischemia determines the secretion of "renin," which is an enzyme and acts on a blood globulin ("hypertensin precursor") and gives rise to a substance ("hypertensin") which produces vasoconstriction. Another enzyme, "hypertensinase," which destroys hypertensin, is present in blood and body tissues. A better understanding of the mechanism of renal hypertension may suggest the treatment of this disease which should aim at suppressing or diminishing the secretion of renin by the kidney, inhibiting the reaction of renin with blood globulin, diminishing the amount of hypertensin precursor and inhibiting the action of hypertensin by increasing the amount or the activity of hypertensinase or some other neutralizing agent. After injection of renin into chloralosed dogs, the hypertensin precursor decreases and even disappears from their blood. After nephrectomy, the hypertensin precursor increases and hypertensinase decreases.

Clinical Experience with Sulfamethylthiazole.—Brown and Herrell review their clinical experience with the use of sulfamethylthiazole in 30 cases of pneumonia, 7 of septicemia, 5 of acute bacterial endocarditis, 5 pelvic infections, 4 osseous infections, 25 cutaneous infections, 13 infections of the ear, nose and throat, 3 urinary infections and 14 cases of miscellaneous infections; a total of 106 cases. The drug was administered orally to the majority of the patients in doses similar to sulfanilamide and sulfapyridine. However, larger doses were frequently used for and tolerated by the severely ill patients. The sodium salt of sulfamethylthiazole was used intravenously for 3 patients and it significantly elevated the concentration of the drug in the blood. Sulfamethylthiazole orally produced concentrations of the free drug in the blood similar to but somewhat lower than those that result from sulfapyridine. A minimal amount of conjugation occurred with sulfamethylthiazole. The results obtained to date from its use seem to substantiate experimental predictions. *Staphylococcus aureus* and *Diplococcus pneumoniae* (type I) infections in particular seem to respond to treatment. With the exception of lower motor neuron involvement in 3 cases and of cutaneous eruptions in 9, toxic effects seemed to be less than those encountered following the use of sulfapyridine and sulfanilamide. Significant nausea and emesis occurred infrequently. The danger of lower motor neuron involvement makes it unwise to use sulfamethylthiazole for mild infections caused by *Staphylococcus aureus*. However, a fulminating infection which carries a high mortality rate far outweighs the danger of toxic manifestations from drug therapy, and this drug or a related preparation may be indicated.

Endemic Riboflavin Deficiency in Children.—During a period of two years Spies and his colleagues examined repeatedly 472 children, from 5 months to 14 years of age, of parents with deficiency diseases. They paid particular attention to their physical and mental development and to the presence or absence of lesions of riboflavin deficiency. They made a clinical diagnosis if one or more of the deficiency lesions ("chei-

losis," the reddened macerated areas at the angles of the mouth and the linear lesions or fissures of the lips and the ocular symptoms characterized by bulbar conjunctivitis, lacrimation, burning of the eyes and failing vision) were present. Cheilosis was observed in 113 cases, linear lesions in 93 and ocular manifestations in 167. These children were usually underweight and underdeveloped for their age. Many were apathetic and indifferent and made poor progress in school. Frequently they complained of sore mouths and burning and itching eyes. The symptoms waxed and waned with the seasons and with changes in the quality of the dietary, but they appeared most frequently during the spring and summer. Increased exercise and infections seemed to precipitate the appearance of lesions in borderline cases. The response of the children to synthetic riboflavin or substances rich in it was gratifying. The cheilosis healed rapidly, the ocular symptoms disappeared and their general health improved. Unless therapy was continued or the diet improved, the disease tended to recur. Dietary studies showed that almost without exception the mothers of these children had subsisted on grossly inadequate diets during pregnancy and lactation, and also that the majority of the infants and children studied received only 35 per cent of the estimated requirement of riboflavin. The average case responded satisfactorily to the oral administration of 1 mg. of riboflavin three times a day, 1 ounce of brewers' yeast or liver extract daily.

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10:651-936 (Oct.) 1940. Partial Index

Technics of Therapy. F. Rosenheim, Boston; N. W. Ackerman and Madeline U. Moore, New York.—p. 651.
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Mental Development of Prematurely Born Children: Critical Review of Literature. A. L. Benton, New York.—p. 719.
Children's Reactions to Discovery of Genital Differences. J. H. Conn, Baltimore.—p. 747.
School Performance of Children Receiving Amphetamine (Benzedrine) Sulfate. C. Bradley and Margaret Bowen, East Providence, R. I.—p. 782.
Analysis of Prolonged Hypomanic Episode in a 5 Year Old Child. D. Beres and Augusta Alpert, New York.—p. 794.
Overt Mass Masturbation in the Classroom. Sonia S. Stirt, New York.—p. 801.
Psychotherapy in Practice. D. A. Thom, Boston.—p. 815.
Psychoanalytic Experiences in Public School Practice. H. Zulliger, Bern, Switzerland; English translation by Gladys V. Swackhamer, Hartsdale, N. Y.—p. 824.

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14:565-756 (Oct.) 1940

*Tetanus Toxoid Immunization in the United States Navy. W. W. Hall, Washington, D. C.—p. 565.
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Vitamins in Peptic Ulcer. H. Field Jr., W. D. Robinson and D. Melnick, Ann Arbor, Mich.—p. 588.
*Prevention of Pernicious Anemia: Recognition of Latent Stage in Relatives. J. M. Askey, Los Angeles.—p. 593.
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Industrial Medicine as a Specialty and Its Relation to General Practice. G. H. Gehrman, Wilmington, Del.—p. 621.
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Direct Nonpenetrating Injuries of Heart. H. D. Leinoff, New York.—p. 653.
*Treatment of Diabetes Mellitus with Four-Meal Diet: Means of Circumventing Certain Difficulties Arising in Use of Protamine Zinc Insulin. H. M. Margolis and V. W. Eisenstein, Pittsburgh.—p. 667.
*Roentgen Treatment of Adrenal Glands in Angina Pectoris, 100 Cases. W. Raab, Burlington, Vt.—p. 688.
Specialization in Internal Medicine. W. B. Breed, Boston.—p. 711.

Tetanus Toxoid Immunization in the Navy.—Hall summarizes the work on active immunization against tetanus which began in 1934 on the fleet hospital of the United States Navy, the U. S. S. *Relief*. Since then 3,446 midshipmen of the Naval Academy as well as other navy personnel and dependents have been immunized. The freedom from reactions in the use of alum precipitated toxoid has been universally noted. Soreness of the arm, disappearing in forty-eight hours or sooner, occurred from injections given intramuscularly. When injections were made subcutaneously a cutaneous reaction occurred which was greater in intensity the closer to the skin the mate-

rial was placed. This was followed by a subcutaneous induration which remained as a nodule for one or two weeks. The intramuscular route was chosen because of its relative freedom from local reaction. It has been suggested that immunity is enhanced when the material is placed in the skin. This has not been the observation in the Navy, as no uniformly higher level of antitoxin titer was observed in those who had a violent cutaneous reaction than in those in whom the injection was made intramuscularly and who had little or no cutaneous reaction. General reaction has been minor, seldom amounting to more than mild malaise and an occasional minor and short rise in temperature. Some reactions were encountered when a certain toxoid was used. The reactions were probably caused by inadequate washing of the alum precipitated toxoid in the course of preparation. No case of tetanus among the immunized individuals has as yet been reported. The actual antitoxin level in the blood is not of prime importance. Basic immunity, or the ability of tissue to react with the production of antitoxin, is the essential condition. The plan adopted in the Navy is to give two injections eight weeks apart as basic immunization, injection at the time of injury, if deemed necessary to raise blood antitoxin rapidly, and injection every four years after basic immunization to maintain immunity at a high level. All midshipmen at the U. S. Naval Academy are now immunized with alum precipitated tetanus toxoid. Such immunization is ideally fitted to the needs of the military services and to other groups which can be well controlled. Its universal adoption in such groups seems inevitable.

Prevention of Pernicious Anemia.—Askey believes that the challenge for the future must be to diagnose pernicious anemia before blood and nervous system changes appear. He presents the accumulating evidence that potential cases are to be looked for in the relatives of patients and suggests a scheme by which they may be recognized in the latent stage. Pernicious anemia has been found in several members of families to an extent far above the expectation from chance alone. Increased frequency of pernicious anemia among relatives should be reflected in an increased incidence of its precursor, anacidity. All the studies of relatives analyzed as to age and the nearness of blood relationship show an increased incidence of anacidity, particularly in the two decades prior to 40, and about a double percentage of anacidity among the near relatives as opposed to distant relatives. Of a total of 174 cases in which previous gastric analyses had been recorded, 171 showed anacidity. Except in rare cases, true anacidity is found in pernicious anemia and must necessarily precede its development. Those relatives with a pernicious anemia genotype should show histamine refractory anacidity for a variable period prior to the manifestation of the anemia. Such a finding justifies at least the suspicion of potential pernicious anemia. The presence of free acid indicates that the risk of the immediate development of the anemia is small. During the last six years the author adopted a tentative scheme for the study of families in which pernicious anemia was present. He arbitrarily accepted heredity as the most important etiologic factor and considered the family as the unit of greatest potential concentration. Ten families were discovered with two or more persons having the disease, and 10 were collected from fellow internists in Los Angeles. In 18 of these 20 families the familial occurrence was proved; in 2 it was based on hearsay. Every patient was told of the familial nature of the disease and requested to have his relatives come in for a histamine gastric analysis. Many relatives refused, but 61 agreed and 10 of these showed anacidity. In the families thus studied, severe crippling pernicious anemia has since developed in 2 relatives who refused to have gastric analyses. Of the 10 anacid relatives, signs or symptoms of early pernicious anemia have developed in 4, hypochromic anemia (apparently idiopathic) in 2, 3 have normal blood and 1 cannot be located. Of the 4 cases believed to be incipient pernicious anemia, 3 were proved to be macrocytic. In 1 the diagnosis was thought justifiable owing to clearcut history of glossitis and paresthesias relieved by liver. The development of hypochromic anemia in 2 cases stresses the tendency of the apparently idiopathic form to appear in pernicious anemia families. Whether there is latent or coexistent

pernicious anemia can only be conjectured. Achlorhydria suggests the importance of knowing whether the patient has or has had a familial history of pernicious anemia. Since pernicious anemia may occur only in a single generation, it would seem important that the patients with achlorhydria be advised of this hereditary tendency so that their grandchildren may be able to make a positive statement regarding its familial occurrence. The physician should study the family rather than the patient alone. The anacid relatives should be watched for early signs and symptoms. It appears unwise to acquaint them with the early symptoms, as it would lead to the promiscuous use of liver and prevent the recognition of the early development. The insidious development of severe spinal cord damage may be prevented in many cases if the relatives of pernicious anemia patients are sought out and grouped by means of the histamine gastric analysis.

Four-Meal Diet for Diabetes Mellitus.—Margolis and Eisenstein point out that, despite technical refinements and improvements in the uniformity and stability of the new insulins, culminating in protamine zinc insulin, frequent failings of their slower actions have become apparent. Their failings are manifest in diurnal glycosuria, in the necessity for supplementary injections of regular insulin, in serious, even fatal, reactions and often in the abandonment of protamine zinc insulin in many cases in which its aid would have been most welcome. The authors were able to circumvent the obstacles by providing optimal dextrose absorption in relation to the action of protamine zinc insulin. Since the maximal depression of the blood sugar level occurs from ten to twenty-four hours after the injection of protamine zinc insulin, an adequate supply of carbohydrate was made available at the time of its greatest need by giving a liberal carbohydrate meal late in the evening, furnishing carbohydrate which is fed into the blood stream during the night slowly and continuously. This four-meal procedure yielded smooth and relatively rapid diabetic control, even in severe cases, and has in their experience successfully averted the most disagreeable features encountered when protamine zinc insulin is used. Diurnal glycosuria was apparently more readily controlled, nocturnal reactions were avoided, the need for supplementary regular insulin was obviated and the simplicity of management with protamine zinc insulin alone, that is a single daily injection, was gained. The records of 14 representative diabetic patients of various ages and with different degrees of illness are cited by the authors in the hope of stimulating a more intensive trial by others. They state that, since a single injection of protamine zinc insulin cannot be placed precisely at points around the clock where food is, the food can be placed, with a high degree of safety, where the greatest insulin action is.

Roentgen Treatment of Adrenals in Angina Pectoris.—Raab advances the theory that attacks of stenocardiac pain on effort, psychic emotion or cold are caused by anoxia of the cardiac muscle. This is largely due to acute discharges of epinephrine from the adrenals occurring physiologically under these conditions. Epinephrine exerts a specific anoxiating effect on the cardiac muscle which under normal circumstances is compensated by simultaneous dilatation of the coronary arteries. This compensatory mechanism must fail when the coronary arteries are unable to dilate adequately because of coronary sclerosis and thus an abnormally exaggerated painful degree of myocardial asphyxia results. Attempts to relieve the symptoms of angina pectoris by restricting the acute discharges of epinephrine through roentgen irradiation of the adrenals were successful in 76 of 100 patients. These patients had typical attacks of angina pectoris on effort, emotion or cold; several of the cases were of the severest kind. Sixty-two patients were entirely or almost entirely freed from complaints or, at least, considerably improved for an average of thirteen and one half months, 14 patients were moderately improved for an average of seven and one half months and 24 patients did not respond. Electrocardiographic signs of myocardial anoxia disappeared partly or completely in most of the successfully treated patients but remained unchanged in those whose complaints were not improved. The blood pressure, either high or normal, remained practically unchanged in all instances.

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- Experimental Studies on Headache: Further Analysis of Mechanism of Headache in Migraine, Hypertension and Fever. A. M. Sutherland and H. G. Wolff, New York.—p. 929.
- Treatment of Unilateral Paralysis Agitans by Section of Lateral Pyramidal Tract. T. J. Putnam, New York.—p. 950.
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- Neuropathologic Study of Six Cases of Psychoses in Which Metrazol Was Used. A. Weil and E. Liebert, Chicago.—p. 1031.
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- Neuropsychiatric Complications Following Severe Loss of Blood. N. Reider, Topeka, Kan.—p. 1069.
- Diffuse Tuberculosis of Pituitary Gland Simulating Tumor, with Post-operative Recovery. C. C. Coleman, Richmond, Va., and J. M. Meredith, Charlottesville, Va.—p. 1076.
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- Decerebrate Tonic Extensor Convulsions as Sign of Occlusion of Basilar Artery: Report of Case with Autopsy. M. Scott and H. C. Lennon, Philadelphia.—p. 1102.
- Cerebral Dysrhythmias in Relatives of Epileptic Persons. L. J. Robinson, Palmer, Mass.—p. 1109.

Archives of Ophthalmology, Chicago

24:867-1076 (Nov.) 1940

- Cataract of Dystrophia Myotonica. J. H. Allen, Iowa City, and C. G. Barer, New York.—p. 867.
- *Hereditary Primary Glaucoma: Pedigree with Five Generations. W. H. Stokes, Omaha.—p. 885.
- Colored Charts as Supplementary Test for Macular Vision: Preliminary Report. S. Engel, San Francisco.—p. 910.
- Tendon Transplantation for Paralysis of External Rectus Muscle: Further Report. S. R. Gifford, Chicago.—p. 916.
- Massachusetts Vision Test: Improved Method of Testing Eyes of School Children. A. E. Sloane, Boston.—p. 924.
- Prechiasmal Syndrome Produced by Chronic Local Arachnoiditis: Report of Three Cases. W. I. Lillie, Philadelphia.—p. 940.
- Sparing and Nonsparing of "Macular" Vision Associated with Occipital Lobectomy in Man. W. C. Halstead, A. E. Walker and P. C. Bucy, Chicago.—p. 948.
- Phakoma Retinae and Adenoma Sebaceum. S. R. Gifford, Chicago.—p. 967.
- Corneal Opacities in the Alaskan Eskimo: Possible Causation. W. L. Mould, San Pedro, Calif.—p. 972.
- Localization of Intra-Ocular Foreign Bodies. D. M. Yazujian, Trenton, N. J.—p. 975.
- Bilateral Subconjunctival Lymphoid Infiltration: Report of Case. A. V. Saradarian, Union City, N. J.—p. 980.
- Peripheral Vascular Picture in Retinitis Pigmentosa. W. M. Brown and E. L. Whitney, Detroit.—p. 984.
- Anticarcinogenic Action of Certain Nitrogenous Factors. Helen S. Mitchell, Gladys M. Cook and Mary D. Henderson, Amherst, Mass.—p. 990.
- Ocular Conditions Associated with Clinical Riboflavin Deficiency. L. V. Johnson and R. E. Eckardt, Cleveland.—p. 1001.

Hereditary Primary Glaucoma.—Stokes reports the occurrence of glaucoma in five generations. The history is as follows: William S., born in 1799, became totally blind fourteen years before his death at the age of 47. Of his two children Joe, who had normal eyes, did not marry; but Elizabeth became blind gradually while still young and for several years before death at the age of 46 she suffered from severe "neuralgic" pains in her head (absolute glaucoma). Five of her 8 children became totally blind in their early twenties. One of these, a woman of 84, is still living. The 4 children of one of these 5 affected patients are not in sympathy with the medical profession and neither they nor their children are available for examination, but of the other 4 patients having 18 children 7 were affected; 4 other children died early (at 14, 9, 6 and 2 years respectively) of typhoid. The children and the grandchildren of the 3 youngest persons of this sibship, the third generation, who did not have glaucoma did not acquire the disease. The fourth generation glaucoma came on during the second, third and fourth decades. Five of the 7 affected persons of the fourth generation married and they had 24 children, of whom 7 had glaucoma

between the ages of 15 and 31. The 6 children of the sixth generation, from 1 to 8 years of age, have been examined when their eyes were apparently normal, but they are as yet too young to have acquired the disease. The author states that hereditary glaucoma appears to result from a simple dominant and not from a sex-linked gene, as the transmission by the two sexes in the foregoing pedigree was equal. As far as he can judge from this pedigree, the chance that an offspring of a glaucomatous person would be similarly affected is about 50:50 and the chance of an offspring of a normal person appears negligible. Consanguinity did not occur in this pedigree. The reduced age of onset in the younger generation must not be taken as proof of a general tendency to anticipation of the disease. Hereditary glaucoma usually, but by no means always, appears in a chronic form. It is possible that a local or general disposition to glaucoma is inherited and the appearance of the disease depends on other factors, either inherited or acquired. The incidence of myopia was sufficiently great to suggest that the hypertension had been influential in producing refractive abnormality. There is no evidence that a beneficial outcome will result without operation. The only permanently good results were obtained in persons having one of the fistulizing operations. The best results were obtained when the operation was performed when glaucoma was still in the compensatory stage; that is, before irreversible secondary anatomic and pathologic changes occurred.

Archives of Physical Therapy, Chicago

21:577-640 (Oct.) 1940

- Physical Therapy Compared with Other Measures in Arthritis. R. L. Cecil, New York.—p. 581.
The Penetrative Effect of Cold. W. Bierman and Mae Friedlander, New York.—p. 585.
Investigations on Influence of Climatologic Factors on Blood Sugar. G. Cronheim, Saratoga Springs, N. Y.—p. 593.
Nasal Ionization: Its Present Clinical Application. C. D. Blassingame, Memphis, Tenn.—p. 602.
Physical Therapy of Various Manifestations of Brucellosis (Undulant Fever). H. J. Harris, Westport, N. Y.—p. 605.
Improved Inhalation Therapy of Asthma. H. A. Abramson, New York.—p. 612.
Technic in Short Wave Therapy. C. O. Molander, Chicago.—p. 615.
Physical Therapy and Bronchoscopy. J. D. Kernan, New York.—p. 620.

Canadian Medical Association Journal, Montreal

43:405-508 (Nov.) 1940

- Water and Electrolyte Balance in Surgery. F. B. Gurd and H. R. Robertson, Montreal.—p. 405.
Postoperative Perfusion of Biliary Ductal System: Preliminary Report. D. Macdonald, St. Catharines, Ont.—p. 411.
*Hypertension in Girl of 12, Associated with Unilateral, Chronic, Atrophic Pylonephritis, Treated by Nephrectomy. F. S. Patch, L. J. Rhea and J. T. Codnere, Montreal.—p. 419.
Nephrotic Syndrome with Hypertension in Diabetes Mellitus. M. A. Simon, Montreal.—p. 425.
Contribution to Anatomy of Ulnar Bursa. C. R. Salisbury, Kingston, Ont.—p. 430.
Cyst of Cavum Vergae. W. Leslie, Winnipeg, Man.—p. 433.
Accidental Bilateral Ligation of Ureters. F. Pilcher Jr. and A. E. Aikenhead, Calgary, Alta.—p. 436.
Carcinoma of Vulva. W. G. Cosbie, Toronto.—p. 439.
Comparative Efficacy of Various Methods for Administering Insulin. E. M. Watson, London, Ont.—p. 444.
Relation of Pulmonary Condition to Bone and Joint Tuberculosis. R. J. Collins and L. Macpherson, St. John, N. B.—p. 448.
Survey of Entozoa in Adults in a Toronto Hospital. E. Kuitunen-Ekbaum, Toronto.—p. 451.
Studies on Pinworm Infection in Canada: I. Incidence of Pinworm Infection in French-Canadian School Children. M. J. Miller and L. Choquette, St. Anne de Bellevue, Que.—p. 453.
*Id.: II. Tests with Gentian Violet in Treatment of Pinworm Infection. M. J. Miller, L. Choquette, W. Audet, R. F. Kelso and J. A. Guenette, St. Anne de Bellevue, Que.—p. 455.
The Psychoneuroses. A. L. MacKinnon, Guelph, Ont.—p. 458.
Diagnostic and Prognostic Value of Sternal Marrow Examination. J. R. E. Morgan, Toronto.—p. 463.
Cancer of Rectum. J. A. MacFarlane, Toronto.—p. 467.
*Fatal Serum Reaction: Case. R. Ferguson, Montreal.—p. 469.

Hypertension in Young Girl Associated with Pylonephritis.—Patch and his colleagues report a case of hypertension in a girl of 12, who was found to have a unilateral atrophic pylonephritis and who has been apparently cured by nephrectomy. At the age of 18 months she had an illness lasting a few days for which a diagnosis of pyelitis was made. Since then she has had intermittent illnesses with nausea, epigastric pain and malaise. Cystoscopy was done when she was 7 because of a pyuria of four months. The right kidney urine contained clumped pus. The left kidney urine was normal. The right

kidney pelvis was lavaged with mercurochrome. Her health improved and she was well until Nov. 11, 1939, when she complained of a dull ache in her left loin. On November 13 she complained of severe occipital headache. Within the next twenty-four hours she was seized with several short convulsions, became unconscious and was admitted to the Woman's General Hospital in Montreal. There were no urinary symptoms. Cystoscopic and pyelographic studies were made showing an atrophic right kidney and a large left kidney. Her blood pressure varied between 180 and 140 systolic, and 135 and 105 diastolic. A right nephrectomy was done on December 27. The pathologic diagnosis was chronic pyelonephritis with secondary atrophy of the kidney, arteriosclerosis, hydronephrosis and chronic ureteritis. There was no appreciable change in the patient's blood pressure up to the time she left the operating table. One hour afterward it was 150; two hours after operation it was 115 systolic and 95 diastolic. During the next twenty-four hours the systolic pressure averaged 125. Following an intravenous infusion of dextrose-saline solution the blood pressure rose to 165 systolic and 130 diastolic and during the next twenty-four hours it gradually fell to 120 systolic and 90 diastolic. She was discharged from the hospital seventeen days after operation. Her blood pressure seemed to be stabilized at 90 systolic and 60 diastolic. She has remained well and without complaints. On the date of her last examination, June 4, she had gained 20½ pounds (9.3 Kg.) in weight. At this time the blood pressure was 96 systolic and 60 diastolic. The authors collected from literature 22 cases in which unilateral nephropathy was associated with hypertension and in which definite improvement followed nephrectomy. Numerous other cases have been mentioned, but with insufficient data to warrant inclusion. Of the 23 cases, 5 occurred in children of 12 or less years of age.

Gentian Violet for Pinworm Infection.—Miller and his collaborators used gentian violet tablets in the treatment of 29 school children, from 6 to 13 years of age, positive for pinworms by the National Institute of Health anal swab technic. The gentian violet was administered in ½ grain (0.03 Gm.) and ¾ grain (0.01 Gm.) tablets. The disintegration of the tablets was supposed to occur four hours after they were swallowed, thus providing the largest concentration of the drug at the site of the infection. Treatment was continued for ten consecutive days. Children from 6 to 9 years of age were given two ¾ grain tablets three times a day before each meal and children from 10 to 13 years of age were given one ½ grain tablet three times a day before each meal. One week following the completion of the treatment an anal swab was made on each patient and two others at weekly intervals. Of the 29 children who took the prescribed dosage and had three post-treatment swabs, only 3 were found still positive following treatment. The effects of gentian violet could be studied on 31 patients taking the entire prescribed dosage. Of these, 23 reported no ill effects, 2 reported slight abdominal pain, 3 slight nausea lasting only one day, 1 anorexia lasting one day, 1 anorexia lasting for several days and 1 colicky pains with nausea. No child in the age group tested and taking the prescribed dosage vomited. However, 2 children (1 and 8 years old was inadvertently given the higher dosage and the other child's dosage was halved) vomited and had anorexia. Both of these children were underweight and had poor appetites, and the smaller child was extremely nervous. The symptoms were usually so mild that treatment was not interrupted with the exception of 4 patients whose symptoms disappeared and did not return with the resumption of treatment.

Fatal Serum Reaction.—Ferguson cites the case of a boy of 6 years who was given 3 minims (0.18 cc.) of tetanus antitoxin because of many deep abrasions covered with street dirt as a result of a car accident. The antitoxin was given at 3:05 p. m., at 3:07 sodium salt of *n*-methyl-cyclohexenylmethyl malonylurea was started intravenously, and in eight minutes 5.5 cc. had been given, which was thought to be enough. There had been no premedication and the patient went to sleep quite easily with some slight twitching. There was no appreciable change in the pulse and only slightly shallower respiration. The color remained good. At 3:20 the patient suddenly began to have trouble getting air into the lungs and would not breathe, although the passage was free. The chest was held in a tightly

contracted state of full inspiration. Artificial respiration was begun and 5 minims (0.3 cc.) of epinephrine was given subcutaneously. The pulse remained strong. At 3:30 a large wheal was noticed at the site of the intradermal injection of the tetanus antitoxin. The whole flexor surface of the forearm from the wrist to the elbow was reddened and edematous. The pulse was becoming irregular and 10 minims (0.6 cc.) of epinephrine was injected subcutaneously, followed by 1.7 cc. of a 25 per cent solution of pyridine betacarboxylic acid diethylamine intravenously. The pulse improved appreciably following this. At 3:45 the pulse again became weaker and 5 per cent dextrose in saline solution intravenously was started. The patient began to take spontaneous breaths of a forced inspirational character and at 3:50 respirations were beginning to be of a more normal character. Large quantities of frothy, blood stained fluid began to pour from the lungs. The intravenous injection was stopped after 350 cc. had been given and the patient was placed in the Trendelenburg position to facilitate drainage. At 4:25 the patient's condition was much improved. Oxygen was being administered continuously through the endotracheal catheter. At 5:30 the patient suddenly stopped breathing and could not be revived. Death was considered to be due to anaphylaxis. The postmortem diagnosis after necropsy was serum reaction (accelerated) with pulmonary edema.

Journal of Immunology, Baltimore

39:265-368 (Oct.) 1940

- Immunologic Reactions in Poliomyelitis. S. Raffel and E. W. Schultz, Stanford University, Calif.—p. 265.
Comparison of Various Physical Means of Liberation of Agglutinin from *Haemophilus Pertussis* in Phase I. E. W. Flosdorf and Anne C. Kimball, Philadelphia.—p. 287.
Studies on Detectability of Pneumococcal Capsular Polysaccharide in Urine: Influence of Variations in μ n. P. F. de Gara and S. C. Bukantz, New York.—p. 297.
Determination of Optimal Ratio of Cholesterol to Tissue Extract Antigen in Complement Fixation Test for Syphilis. J. F. Kent, Albany, N. Y.—p. 307.
Proteins and Antibodies of Serum After Prolonged Dialysis: I. Periodic Removal of Precipitates. S. Raffel, C. F. Pait and M. C. Terry, Stanford University, Calif.—p. 317.
Id.: II. Dialysis Without Periodic Removal of Precipitate. S. Raffel and M. C. Terry, Stanford University, Calif.—p. 337.
Id.: III. Serial Immunization with Quantitative Antibody Estimations. S. Raffel and M. C. Terry, Stanford University, Calif.—p. 349.
Hemolytic Effect of Typhoid Cultures in Combination with Pure Lines of Bacteriophage. F. Schiff and S. Bornstein, New York.—p. 361.

Journal of Investigative Dermatology, Baltimore

3:347-442 (Oct.) 1940

- Hereditary Influences in Psoriasis. C. Lerner, New York.—p. 347.
Nails and Nail Changes: III. Brittleness of Nails (*Fragilitas Unguium*). H. Silver and B. Chiego, New York.—p. 357.
*Studies of Transmissibility of Syphilis: Infectiousness of Vaginal Secretions and Menstrual Blood of Syphilitic Women. H. Pariser, Philadelphia.—p. 375.
Studies with Antigens: VI. Significance of Scratch Test Reactions to Purified House Dust Extracts. B. G. Efron, C. H. Boatner and M. R. Pabst, New Orleans.—p. 401.
Value of Liver Extract in Cases Intolerant to Arsenicals, Heavy Metals and Radiation. G. M. MacKee and G. D. Astrachan, New York.—p. 409.

Transmissibility of Syphilis.—Pariser investigated the infectiousness for rabbits of the vaginal secretions and menstrual blood of 30 untreated syphilitic women. The biologic method of animal inoculation used is detailed. The author considered a result positive only when the injected material produced a syphiloma containing many spirochetes. The vaginal secretions of 7 women produced syphilis in animals. Five of these showed local cervical lesions. The clinical manifestations of the disease in these instances varied from about one week to six and one half years. The sixth positive result was obtained from the menstrual blood of a woman with secondaries who had no local cervicovaginal lesions, and the seventh from an early secondary syphilitic pregnant woman whose cervix was edematous, bluish and boggy but with no visible open lesions. How much of this cervical picture was due to the pregnancy is difficult to determine. It might have been the type of early lesion stressed by Stookey, Davies and MacDonald. Initial dark field examination revealed a few organisms which closely conformed to the universally accepted morphology of *Spirochaeta pallida* in 4 cases, slightly thicker

organisms than average but which by subsequent animal inoculation were proved to be *Spirochaeta pallida* in 2 instances while the seventh case was negative. In the absence of lesions the dark field examination in 50 per cent of the cases revealed spirochetes easily distinguished from *Spirochaeta pallida*. The case material consisted of 76 per cent early syphilis and 24 per cent late syphilis. Serologic tests for syphilis in rabbits gave, with certain modifications, high sensitivity ratings but also produced a definite percentage of nonspecific positive serologic tests. These tests should be used only as collateral evidence and only the appearance of a syphiloma containing many spirochetes should be diagnostic. The author concludes that virulent spirochetes are discharged in the syphilitic woman into the vagina in the presence of early or chronologically late (more than four years) local lesions as a relapsing phenomenon. In the absence of such lesions in the early syphilitic woman they are discharged through the menstrual blood or from an abnormally appearing cervix in which it is probable that lesions are present within the cervical os or uterus. Infectiousness through the vagina is periodically recurrent rather than continuous and depends on the presence or absence of local lesions. The physiologic secretions are not infectious. The absolute end point or the frequency of cervical relapse cannot be given, but the author states that in his cases infectious cervical relapse occurred at least six and a half years after definite onset of the disease.

Journal-Lancet, Minneapolis

60:479-522 (Nov.) 1940

- Subdural Hematoma. A. L. Saks, Iowa City.—p. 479.
Surgery of Gallbladder Tract, Based on Understanding of Physiologic Functions and Pathologic Changes that Take Place in the Liver. W. A. Delaney, Mitchell, S. D.—p. 482.
Eye Health Among College Students. J. H. Kler, New Brunswick, N. J.—p. 487.
Blood Transfusions in Pediatrics. W. S. Sako and A. V. Stoesser, Minneapolis.—p. 491.
Summary of a Ten Year Tuberculosis Control Program. L. S. Jordan, Granite Falls, Minn.—p. 502.
Spontaneous and Surgical Covering of Raw Surfaces. J. B. Brown and L. T. Byars, St. Louis.—p. 503.

Journal of Urology, Baltimore

44:389-544 (Oct.) 1940

- Primary Echinococcosis of Kidney. W. A. Barrett, Pittsburgh.—p. 389.
*Bilateral Renal and Ureteral Agenesis. K. B. Grim, Charlottesville, Va.—p. 397.
Renal Tuberculosis and Sanatorium Care. F. H. Colby, Boston.—p. 401.
Retro-Aortic Renal Vein. G. Yelin, Newark, N. J.—p. 406.
Renal Vascular Pedicle: Anatomic Study of 430 Body Halves. J. W. Pick and B. J. Anson, Chicago.—p. 411.
Relationship of Benign and Malignant Hypernephroid Tumors of Kidney: Clinical and Pathologic Study of 77 Cases in 12,885 Necropsies. D. D. Kozoll and J. D. Kirschbaum, Chicago.—p. 435.
Retrocaval Ureter: Report of Case with Operative Correction of Defect. H. C. Harrill, Greensboro, N. C.—p. 450.
Operative Technic in Treatment of Vesical Diverticula. H. H. Young, Baltimore.—p. 458.
Vesical Diverticulectomy. J. E. Dees, Durham, N. C.—p. 466.
Contracture of Bladder: II. Elastosis of Bladder. J. H. Winer, Cleveland.—p. 485.
Prostatic Obstruction as Presenting Symptom of Acute Monocytic Leukemia. S. A. Flaherty, Detroit; H. E. Cope, Lansing, Mich., and H. A. Sheeket, Eloise, Mich.—p. 488.
Frequency of Tubercle Bacillus in Urine of Chronic Pulmonary Tuberculosis in Relation to Urogenital Complications. Esther Rosencrantz, San Francisco.—p. 498.
Clinical Study of 480 Cases of Urinary Lithiasis. H. L. Harrington, San Francisco.—p. 507.
Effect of Intraprostatic Injection of 1 and 1.5 per Cent Aqueous Mercurochrome into Prostates of Dogs. L. W. Riba, B. W. Milligan and F. B. Queen, Chicago.—p. 520.
Content of Male and Female Hormone in Urine of Patients with Prostatic Hypertrophy. Elisabeth Dingemans and E. Laqueur, Amsterdam, Netherlands.—p. 530.
Use of Sulfathiazole and Sulfamethylthiazole in Treatment of Gonorrheal Urethritis. T. M. Burkholder and F. Bang, Baltimore.—p. 541.

Bilateral Renal and Ureteral Agenesis.—Grim cites a case of bilateral renal and ureteral agenesis in the presence of an otherwise normal urogenital system and with no demonstrable developmental defects elsewhere. The patient's mother, a 32 year old multipara, went through a normal gestation until two days before admission to the hospital, when she had abdominal cramps radiating anteriorly from both flanks. No fetal movements could be felt and no heart sounds heard. Several hours after admission she was delivered of an apparently normal

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but slightly macerated stillborn fetus approximately 8 months old. Careful examination of the umbilical cord and placenta revealed no abnormalities. Necropsy of the infant revealed no abnormalities other than the absence of the kidneys and ureters. Embryologically this finding may be due to (1) failure of the ureteral bud to appear, (2) failure of the ureteral bud to develop or grow cephalad into the nephrogenic cap, (3) degeneration of the ureteral bud from any cause before it has contacted the nephrogenic cap, (4) failure of the nephrogenic cap to appear, and (5) degeneration of the nephrogenic cap after its appearance and (6) defective germ plasm. The author points out that Ranier's contention that development of the metanephrogenic blastema depends on the stimulus evoked by cephalic progression of and contact with the ureteral bud seems to be borne out by the observations in his case. He believes the associated pathologic changes may be attributed to asphyxia in utero.

Medical Annals of District of Columbia, Washington

- 9:333-370 (Oct.) 1940
Inclusion Blennorrhea in Pediatric Practice. S. W. Giddens, Toronto, and W. A. Howard, Washington.—p. 333.
Prenatal Care. H. F. Kane, Washington.—p. 342.
Failures and Recurrences Following Estrogen Treatment of Gonorrheal Vulvovaginitis. B. Notes, Washington.—p. 346.
Value of Roentgenography in Diagnosis and Localization of Intestinal Obstruction. A. M. Cove, Brooklyn, and M. Silverman, Washington.—p. 348.

Military Surgeon, Washington, D. C.

- 87:289-400 (Oct.) 1940
Surgical Pathology of Acute Infections of Maxillofacial Area: Clinico-Anatomic Study. M. W. Carr.—p. 289.
Infantile (Acquired) Hernia at Umbilicus in Soldiers. H. H. Parsons.—p. 298.
Intravenous Anesthesia and How to Use It. R. B. Phillips.—p. 301.
Experimental Aircraft-Submarine Litter and Transportation Splints. W. L. Mann and R. Kaysen.—p. 305.
Mechanized Medical Units. C. M. Hendricks.—p. 311.
Thoraco-Abdominal Syndromes. M. B. Shimkin.—p. 316.
Acute Gangrenous Diverticulitis (Meckel's) with Perforation Due to Fish Bone: Case. J. M. Tamraz.—p. 328.
Short Wave Diathermy. L. De Forest.—p. 330.
Allergy in Military Medicine. F. G. Crandall Jr.—p. 337.
Early Panama Crossings. J. M. Phalen.—p. 352.

Nebraska State Medical Journal, Lincoln

- 25:393-428 (Nov.) 1940
Present Social Trends and Future of Medicine. E. J. McCormick, Toledo, Ohio.—p. 393.
*Intramuscular Administration of Sodium Sulfapyridine: Preliminary Report. L. T. Hall, C. E. Thompson and R. J. Wyrens, Omaha.—p. 398.
Impalement of Rectum with Intra-Abdominal Rupture: Report of Three Cases. M. C. James, Columbus.—p. 399.
Treatment Facilities in the State Mental Hospitals in Nebraska. J. C. Nielsen, Ingleside.—p. 403.
Traumatic Surgery as a Specialty. T. E. Riddell, Scottsbluff.—p. 409.
Practical Consideration of Antianemic Drug Therapy: Uses and Abuses. J. C. Sharpe, Omaha.—p. 413.
Simultaneous Rupture of Left Kidney and Spleen: Case Report. P. S. Adams and W. F. Bowers, Omaha.—p. 417.
Standards for Judging a Member of a Profession—The Physician. E. C. Sage, Omaha.—p. 419.

Sodium Sulfapyridine Intramuscularly.—Hall and his associates observed no local irritation or tumefaction after many deep intramuscular administrations of sulfapyridine. The clinical effects were equal to those obtained by other routes. Blood levels of from 3 to 10 mg. per hundred cubic centimeters were promptly obtained. Once the level is reached it can be maintained for longer periods than when given intravenously. Gastrointestinal reactions are almost entirely avoided, nausea does not occur and vomiting is seldom observed. This route may be found to be a safe alternative for intravenous injection in old persons with tortuous and sclerotic vessels, in infants, children and women with inconspicuous veins, or in persons with fat arms. The authors used a 33½ per cent solution of sulfapyridine in sterile water, injecting it deep into the gluteal or thigh muscles. No material must be deposited in the subcutaneous tissue through the needle tract either on injection or during withdrawal of the needle. Each cubic centimeter of the solution contains 0.33 Gm. of the drug. From 6 to 10 cc. was given as the first injection and was followed by 3 cc. every four hours until the temperature had been normal for twenty-four hours. Thereafter the dose was reduced by one half and continued for

the next five or six days. This route has been used for pneumonia, undulant fever, appendicitis with peritonitis, abscesses, pyelitis, typhoid, gonorrhea, sinusitis and many other diseases. The authors state that the clinical results parallel those obtained by orally administered sulfapyridine.

New York State Journal of Medicine, New York

- 40:1419-1486 (Oct. 1) 1940
Diagnosis of Serious Urologic Conditions. H. H. Young, Baltimore.—p. 1425.
Treatment of Epithelial Tumors of Bladder with Radiation. A. L. Dean and J. Balfour, New York.—p. 1431.
Treatment of Tumors of Bladder by Refrigeration. A. McCravy, Philadelphia.—p. 1435.
General Considerations in Surgical Treatment of Carcinoma of Bladder with Particular Reference to Total Cystectomy. J. T. Priestley, Rochester, Minn.—p. 1441.
Administration of Sulfapyridine and Its Congeners in Pneumonias. J. G. M. Bullowa, H. D. Ratish, A. Davidson and Constance Lebar, New York.—p. 1450.
Influence of Sulfapyridine on Pneumonias of Childhood: Clinical Study of Eighty-Five Cases at a Municipal Hospital. S. L. Ellenberg and H. S. Altman, New York.—p. 1457.
Survey of Eighteen Years of Pneumonia at the Nassau Hospital. B. R. Allison, Hewlett.—p. 1464.

40:1487-1556 (Oct. 15) 1940

- Participation in Public Health Program: Public Health Personnel. V. A. Van Volkenburgh, Albany.—p. 1493.
The Place of the Medical Profession in the Public Health Program. A. N. Thomson, Brooklyn.—p. 1498.
The Citizen. K. D. Widdemer, New York.—p. 1501.
The School Physician in the Public Health Program. G. M. Wheatley, New York.—p. 1506.
Aseptic Total Colectomy. D. P. MacGuire, New York.—p. 1515.
Hyperactive Carotid Sinus Reflex Syndrome. A. Koffler and S. Alexander, New York.—p. 1519.
Sulfapyridine in Meningococcal Meningitis: Review of Literature and Report of Case. H. I. Kantor, New York.—p. 1526.
Obstetric Prognosis and Treatment on Basis of Pelvic Architecture. A. Weinberg, Far Rockaway.—p. 1530.

South Carolina Medical Assn. Journal, Greenville

- 36:301-330 (Nov.) 1940
Chronic Conditions of Gallbladder. Gertrude Holmes and H. Smith, Greenville.—p. 301.
Surgical Management of Varicose Veins and Ulcers. H. G. Smyth, Charleston.—p. 307.

Southern Medical Journal, Birmingham, Ala.

- 33:1117-1240 (Nov.) 1940
Reticulo-Endotheliosis. J. H. Lamb and H. A. Stout, Oklahoma City.—p. 1117.
Use and Abuse of Theophylline and Its Derivatives. A. McMahon and R. A. Nussbaum, St. Louis.—p. 1127.
Role of Streptococcus in Some Dental Infections: Study of Residual Areas. Iva C. Youmans and Laura M. Hobbs, Miami, Fla.—p. 1140.
Controlled Rotation Osteotomy of Tibia. D. H. O'Donoghue, Oklahoma City.—p. 1145.
Isolated Bilateral Fracture of First Rib: Case with Unilateral Horner's Syndrome. J. Kulowski and J. H. Ryan, St. Joseph, Mo.—p. 1149.
*Placenta Accreta: Case Report. C. E. Bosshardt, San Antonio, Texas.—p. 1152.
Pyuria: Its Significance in Upper Urinary Tract Disease. H. J. Lindner, New Orleans.—p. 1155.
Treatment and Prevention of Deafness in Children. J. E. Bordley, Baltimore.—p. 1159.
Cataract Attributable to Use of Dinitrophenol. A. O. Pingst, Louisville, Ky.—p. 1164.
Epidemic Diarrhea of Newborn. T. G. Folsom and G. M. Lyon, Huntington, W. Va.—p. 1167.
*Report of Two Ruptured Gastric Ulcers and One Ruptured Duodenal Ulcer in Three Newborn Infants. A. G. Quinn, Memphis, Tenn.—p. 1171.
Dihydratichysterol, Parathormone and Vitamin D₂: Comparison of Their Values: Treatment of Post-Thyroidectomy Hypocalcemic Tetany. D. H. Poer, Atlanta, Ga.—p. 1174.
Comparison of Skin Reactions Obtained by Use of Brucella Nucleoprotein (Brucellergen) and Heated Brucella Organisms in Sensitized Individuals. A. E. Keller, Nashville, Tenn.—p. 1180.
Therapeutic Effects of Aminophyllin in Asthma. A. G. Brown 3d and W. B. Blanton, Richmond, Va.—p. 1184.
Relationship of Personality Changes to Facial Neuralgia. M. S. Love and D. C. Wilson, University, Va.—p. 1186.
Cause and Prevention of Loss of Teeth. C. C. Bass, New Orleans.—p. 1193.
Birth and Early History of the Southern Medical Association. J. L. Crook, Jackson, Tenn., and W. W. Crawford, Hattiesburg, Miss.—p. 1195.

Placenta Accreta.—Bosshardt states that placenta accreta is being seen and recognized more frequently as the most serious complication of the third stage of labor. The condition results from a partial or complete absence of decidua basalis. Placenta

accreta must never be confused with the rather common simple placental retention seen in hour-glass constriction or from some failure of the normal separating mechanism of a healthy placenta in a normal uterus. Since this condition can never be detected before delivery, it should be constantly kept in mind after the second stage of labor. Treatment depends on prompt recognition. Early hysterectomy is the accepted treatment, preceded and followed by blood transfusion, if indicated, and the usual supportive agents for shock. Manual extraction of densely adherent placentas by hand, with placental forceps or by curet is extremely dangerous and predisposes to fatal hemorrhage or puncture of the uterus. In 11 cases treated by supravaginal hysterectomy with no attempts at extraction of the placenta there were no deaths. There were 6 deaths among 30 cases in which abdominal hysterectomy after partial manual extraction was employed. Manual extraction or curettage without hysterectomy for 31 cases resulted in 20 deaths. The combined mortality of the treated series reported in 1931 showing 86 cases with 32 deaths was 37.2 per cent. The author's cases bring the total to 101. His patient, even after procrastination for nine days and adopting the hazardous method, unknowingly, of partial manual extraction, recovered after a subtotal hysterectomy.

Ruptured Ulcers in Infants.—Quinn reports 3 fatal cases of ruptured gastrointestinal ulcers in infants. Two of them occurred during a year when there was an epidemic of infectious diarrhea. One of these, the author believes, can be said to have occurred from this cause. The following diagnostic criteria stand out: First, pneumoperitoneum was determined by roentgen study, yet this failed in the first case so examined. The other diagnostic point was that abdominal distention occurred suddenly in an otherwise healthy infant. The distention was symmetrical and had the feel and appearance of an inflated round bag. The principal features of the first case were an infant doing well who vomited following a feeding and four hours later vomited again. The abdomen was markedly distended, giving the appearance of an inflated ball. Attempts to relieve distention were unsuccessful. Respiratory distress, cyanosis and shock were present. In the second case, because of sudden vomiting, abdominal distention and shock, the presumed diagnosis was ruptured gastrointestinal ulcer, but because pneumoperitoneum was absent on roentgen study the preoperative diagnosis was intestinal obstruction. The operative observations proved the first premise correct, yet no pneumoperitoneum was present. The third infant died five days after operation. The anatomic diagnosis was primary, perforated acute peptic ulcer (clinical), generalized fibrinous purulent peritonitis and bilateral bronchopneumonia. The cause of death was bronchopneumonia.

Tennessee State Medical Assn. Journal, Nashville

33:419-458 (Nov.) 1940

- Treatment of Wounds of Face. R. A. Daniel Jr., Nashville.—p. 419.
Treatment of Fractures of Neck of Femur. E. D. Newell, J. M. Frere and J. M. Higginbotham, Chattanooga.—p. 427.
Head Injuries. R. G. Waterhouse, Knoxville.—p. 432.
Treatment of Injuries of Chest. D. Carr, Memphis.—p. 438.

Virginia Medical Monthly, Richmond

67:655-716 (Nov.) 1940

- Management of Acute Appendicitis: Arguments and Controversies. H. B. Stone, Baltimore.—p. 655.
Treatment of Sinusitis. W. C. Bowers, New York.—p. 660.
Degenerative Neuropsychiatric Conditions Due to Aging Process. R. S. Crispell, Durham, N. C.—p. 668.
Unusual Tumors and Tumor-like Lesions of Spinal Canal and Its Contents, with Special Reference to Pitfalls in Diagnosis. J. M. Meredith, Charlottesville.—p. 675.
Cysts of Maxillary Sinus. T. E. Hughes and J. S. Dryden, Richmond.—p. 687.
Treatment of Ulceration of Foot in Advanced Arteriosclerosis. B. L. Boynton, Norfolk.—p. 689.
Chronic Atonic Dilatation and Hypersecretion of Stomach Successfully Treated with Insulin. W. J. Mallory, Washington, D. C.—p. 691.
Foreign Body Stimulating Gastric Carcinoma. B. Lidman, Norfolk.—p. 693.
Venesection in Pulmonary Edema: Case Report with Discussion of Diagnosis, Etiology and Treatment. G. Geyerhahn, Wilmington, N. C.—p. 696.
Perforated Peptic Ulcer and Recovery Without Operation. H. G. Hadley, Washington, D. C.—p. 697.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

48:591-644 (Oct.) 1940

- *Pyelitis of Pregnancy and Its Management in 121 Cases. R. D. Mussey and S. B. Lovelady, Rochester, Minn.—p. 591.
Simple Method of Therapeutic Abortion Combined with Sterilization. H. C. Falk and A. Shukuris, New York.—p. 597.
Obstetric Forceps. C. H. Davis, Wilmington, Del.—p. 601.
Use of Testosterone Propionate in Gynecologic and Obstetric Disorders. T. E. Mandy and A. J. Mandy, Baltimore.—p. 604.
Dangers and Uses of Radium in Treatment of Carcinoma of Uterus. M. D. Sachs, Portland, Ore.—p. 609.
Kahr Operation for Senile Prolapse. J. H. Clark, Los Angeles.—p. 616.
Surgical Pathology of Thyroid Gland. A. C. Broders, Rochester, Minn.—p. 620.
Further Observations on Thyrotropic Activity of Anterior Pituitary. W. O. Thompson, Phebe K. Thompson and S. G. Taylor 3d, Chicago.—p. 633.
The Heart in Hyperthyroidism. E. J. Kepler, Rochester, Minn.—p. 636.

Pyelitis of Pregnancy and Its Management.—According to Mussey and Lovelady, among 5,960 deliveries at the Mayo Clinic 117 were complicated by pyelitis. Four others have been encountered since the introduction of sulfanilamide. Seventy-two of the patients were primigravidas and forty-five multigravidas, bearing out some previous reports that pyelitis occurs more frequently among the former. There were ninety-two instances of antepartum and twenty-five of postpartum pyelitis. Postpartum pyelitis was usually of mild degree and did not exhibit the usual symptoms of pyelitis of pregnancy. Previous infection of the upper part of the urinary tract plays a part in the recurrence of pyelitis in subsequent pregnancies; however, only twelve of the present patients gave a history of pyelitis prior to the first pregnancy and none gave a history of urinary infection in childhood. The data of the 117 cases do not confirm the assertion that pyelitis increases the hazard of pregnancy. There were four spontaneous abortions and two premature labors. Labor was induced because of pyelitis in seven cases, but not before viability. One of 117 patients died. Acute pyelitis was rarely the cause of preeclamptic toxemia or eclampsia among the series discussed. Although pyelitis is not a common complication of pregnancy it occurs with sufficient frequency to necessitate alert diagnosis and treatment before permanent renal damage occurs. Whenever pus is found in a specimen of urine during periodic prepartum examination a specimen of urine obtained by catheterization should be examined for pus, for pyelitis without subjective symptoms may be present. The 121 patients have been divided into four groups. Group 1 received large quantities of fluids and usually one of the urinary antiseptics, group 2 was treated by ureteral catheter drainage, group 3 was given one of the various mandelic acid preparations and group 4 includes the four patients given sulfanilamide. The results of administering large quantities of fluid to sixty-four patients were uniformly good and indicate that in more than one half of the cases pyelitis of pregnancy will respond favorably to forced fluids and rest in bed. These measures were most effective when applied early in the course of the disease. In group 2, forty-eight patients, there were acutely ill patients who failed to respond to the treatment outlined in group 1, and indwelling catheters were inserted for adequate drainage of the renal pelvis. From 1924 to 1933 ureteral drainage was used in approximately 57 per cent of patients with proved pyelitis of pregnancy. Since 1933 this treatment has been employed in approximately 19 per cent of the cases. When pyelitis of pregnancy is recognized and treated in its early stages, a majority of patients will recover following a regimen of rest in bed, sedatives and forced fluids. The effect of this management has been a continuing decrease in the number of patients requiring ureteral catheterization. Since the advent of chemotherapy, this will no doubt become still less. The only death of the entire series occurred in this group. Mandelic acid was used for the five cases of group 3, and the response to treatment was uniformly good. The response of the four patients of group 4 to sulfanilamide was good. Further observation may indicate the advisability of employing azosulfamide or other allied products. The average duration of fever and hospitalization of the groups of patients was, respectively, fever 3.6, 6.8, 3.0 and 5.0 days, and hospitalization 10.7, 10.8, 14.0 and 13.0 days.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Journal of Mental Science, London 86:751-1064 (Sept.) 1940

- Diphasic Vascular Variation in Treatment of Mental Inefficiency Arising from a Common Somatic Cause. T. C. Graves.—p. 751.
Role of Sex Hormones in Psychiatry. M. Reiss.—p. 767.
Specific Psychotic Reaction of Schizophrenics to Physical Illness. R. E. Hemphill and E. Stengel.—p. 790.
Studies in Certain Pathophysiologic and Psychologic Phenomena in Convulsion Therapy. R. E. Hemphill.—p. 799.
Cerebral Fat Embolism as Cause of Death in Case of Schizophrenia Treated with Triazol (Azoman). G. S. Nightingale and A. Meyer.—p. 819.
Forced Grasping and Disturbances of Attention. B. Schlesinger.—p. 827.
Morbidity Attention: Factor in Nervous Disorder. I. C. K. Mackenzie and Ivy Mackenzie.—p. 839.
Modern Treatment of Epilepsy: Critical Survey, with Special Reference to Sodium Diphenyl Hydantoinate and Comparison of Its Effects with Those of Other Anticonvulsants. D. Blair.—p. 888.
Psychotherapy in Mental Hospital Practice: Being the Preliminary Report of a Full Time Psychotherapist in a Public Mental Hospital. J. Bierer.—p. 928.
Commentary on Case of Acute Systematized Hallucinations: Recorded by the Patient as "The Report of a Nightmare." M. J. Nolan.—p. 953.
Some Points in Technic of Insulin Therapy of the Psychoses. R. Fraser and W. Sargent.—p. 969.
Severe Toxic Effects of Sodium Diphenyl Hydantoinate in Mentally Defective Epileptics. B. A. M. Williamson.—p. 981.
Recent Hysterical States and Their Treatment. A. Kennedy.—p. 988.

Journal Obst. & Gynaec. of Brit. Empire, Manchester 47:365-492 (Aug.) 1940

- Cold Pressor Test in Pregnancy. F. J. Browne.—p. 365.
External Hysterography: Graphic Study of Human Parturient Uterus and Effect of Various Therapeutic Agents on It. M. P. Embrey.—p. 371.
Investigation into Result of Operation in Genital Prolapse. J. Stallworthy.—p. 391.
Eclampsia: Clinical and Biochemical Study: Part II. Biochemical Investigation of Eclampsia. A. S. M. Nayar.—p. 404.
Calcification of Human Placenta. M. Masters and S. G. Clayton.—p. 437.
Treatment of Retroversion of Uterus: Impression of Present Position from Analysis of Cases Undergoing Operation at Samaritan Hospital, London. A. H. Charles.—p. 444.
Desmoplastoma Ovarii Malignum. B. Solomons and G. C. Dockeray.—p. 451.
Unusual Case of Breech Presentation of Eight Months' Pregnancy Complicated by Tubo-Ovarian Abscess. V. R. Merajkar and B. L. Kapur.—p. 455.

47:493-596 (Oct.) 1940

- Relaxation of Pelvic Joints in Pregnancy: Pelvic Arthropathy of Pregnancy. J. Young.—p. 493.
Inversion of Uterus. P. Das.—p. 525.
Prognosis for Fetus in Toxemias of Late Pregnancy. F. J. Browne and Gladys H. Dadds.—p. 549.
Retroperitoneal Cyst Containing Ovarian Remnants: Case. S. Way.—p. 553.
*Cyclic Ulcerative Vulvitis and Stomatitis. O. V. Jones.—p. 557.
Tubo-Uterine Implantation Followed by Successful Pregnancy. S. Hayes.—p. 563.

Cyclic Ulcerative Vulvitis and Stomatitis.—Jones points out that numerous cases of coexisting oral and genital ulceration have been reported but that only 3 of these seemed to have any relation to menstruation. He reports the fourth case of such an association. The clinical similarity between the genital and oral ulcers is striking, and so it is probable that the ulceration of the two areas has the same pathology. Since the original observation by Neumann in 1895 the etiology of their association has excited much discussion and at present there are three main theories: that of an acute infectious dysfunctions, and that of angioneurotic gangrene due to ovarian dysfunction. The first two theories fail to become established. The ovarian dysfunction theory becomes feasible as in the cases reported and in the author's case the lesions were dependent on the menstrual cycle. The condition was associated in some weeks before menstruation, lasting over the period but ceasing after menstruation, while the oral lesion occurred from one to two days before, during or after menstruation. The striking appearance and disappearance of the lesions with a regular relation to menstruation is highly suggestive of an endocrine changes (proliferation of the stratum germinativum, with

increase in the number of young epithelial cells in the basal philic zone of the epithelium, and this is associated with occasional mitosis and a definite leukocytosis and hyperemia) in the vagina related to the hormone changes of menstruation. The fact that the time of these changes coincides with the ulcerative phase in the condition under discussion further enhances the endocrine basis. Since these ulcers appear at the premenstrual period when the secretion of estrogen is highest and disappear at the postmenstrual phase when it is lowest, a deficiency of estrogen is probably not the etiologic factor, and it is unlikely to be due to an excess of estrogen as the phenomena disappear during pregnancy. On the other hand, the absence is present during the stage when the pituitary normally lessens its production of gonadotropic substance and its reaches its maximal concentration. Likewise during pregnancy (as in 1 case) when the anterior pituitary hormone attains its highest degree of activity there was a spontaneous disappearance of the ulceration. Therefore it seems reasonable that a lowered pituitary activity may cause the condition. Ziserman reported great improvement in his case after administration of an anterior pituitary preparation. In the author's case complete relief was obtained with gonadotropic substance, while the anterior pituitary preparation was given was she completely free from both ulcerative lesions. Though the therapeutic trials suggest that deficiency of gonadotropic substance is the basic cause, the true underlying factors must still remain obscure. It is probably due to some systemic condition associated with an imbalance between various hormones. This is plausible, as the ulceration occurs at a time when there is a change in the cycle and when a harmonious cooperation between the hormones is necessary. Therefore any endocrine imbalance that occurs will reflect itself on the changes in the genitalia and general systemic system, and this will be more likely to occur in individuals whose vasodilatory system is easily affected, resulting in ulceration of the mucous membrane. The condition described is a definite syndrome and can be recognized as such when other factors (infection and anemia) have been eliminated. The disease differs from ulcer vulvae in that it is recurrent and rebellious to treatment and appears to be a systemic condition dependent on some dysendocrinism.

Journal of Pathology and Bacteriology, Edinburgh 51:169-316 (Sept.) 1940

- Fundamental Lesion in Acute Diffuse Intracapillary Glomerulonephritis. J. S. Dunn.—p. 169.
Physiologic and Serologic Characteristics of Staphylococci of Human Origin. R. Christie and E. V. Keogh.—p. 189.
Toxin of *Corynebacterium Ovis*. H. R. Carne.—p. 199.
Medial Defects in Circle of Willis and Their Relation to Aneurysm Formation. L. E. Glynn.—p. 213.
Pathologic Changes Produced in Rats and Mice by a Toxic Fraction Derived from *Bacterium Typhi Murium*. G. R. Cameron, M. E. Delafield and Joyce Wilson.—p. 223.
Nature of Human Leukemia: Evidence from Culture of Bone Marrow Cells in Vitro. M. C. G. Israëls.—p. 235.
Pathogenicity and Toxicity of *Bacterium Alkaliscens* for Laboratory Animals. D. G. f. Edward.—p. 245.
*Comparative Study of Anaerobic Strains of Actinomyces from Clinically Normal Mouths and from Actinomycotic Lesions. H. R. Sullivan and N. E. Goldsworthy.—p. 253.
Silicotic Nodule in Human and Experimental Silicosis: Comparative Study. T. H. Belt, A. A. Ferris and E. J. King.—p. 263.
*Pneumoconiosis in Coal Trimmers. J. Gough.—p. 277.
Importance of Suspending Fluid Used in Virulence Tests on *Corynebacterium Diphtheriae*. H. D. Holt and H. D. Wright.—p. 287.

Strains of Actinomyces from Normal and Actinomycotic Mouths.—In an investigation of patients with actinomycotic lesions in the cervicofacial region, Sullivan and Goldsworthy were impressed by the frequency with which the theory of endogenous infection. They have since examined material from the mouths of subjects with no history or clinical signs of actinomycosis and pus from cervicofacial lesions. From these they isolated anaerobic strains similar to *Actinomyces bovis* (Wolff and Israël) and compared these apparently non-pathogenic strains with those obtained from the lesions and with a strain from a subcutaneous abscess secondary to pulmonary actinomycosis. Five strains were isolated from periodontal

pockets (more than 100 were examined) and one from a carious tooth (twenty-four specimens were examined). Five other strains were isolated from lesions situated near the angle of the mandible, and one relatively old strain was obtained from the lesion secondary to pulmonary actinomycosis. In a comparative study which included fermentation reactions, these two groups of strains were identical. The results support the conclusions of other workers that the micro-aerophilic *Actinomyces* of Wolff-Israel is to be regarded as part of the normal flora of the oral cavity, at least if local dental conditions (caries and periodontitis) are accepted as practically universal. The authors' observations at dental clinics suggest that the acute form of actinomycosis is a not infrequent sequela to surgical manipulation of the mouth parts, especially the teeth. Therefore they believe that the organism leads a saprophytic existence in the mouth and invades the tissues only when conditions are rendered favorable, as by injury.

Pneumoconiosis in Coal Trimmers.—Gough states that in the last ten years fifteen coal trimmers have been encountered in routine postmortem work at the Cardiff Royal Infirmary. Three of these had previously been coal miners, but of at least five pneumoconiosis was the main cause of death. Coal trimming is the shifting and storing of coal on board ship in such a way as to make the vessel seaworthy. Most of the work is done in the ship's hold in an atmosphere thick with coal dust. The author's experience in Cardiff with steam coal leads him to conclude that exposure to these high concentrations for many years may lead to serious and sometimes fatal pulmonary fibrosis. One of the five men whose death was attributable to pneumoconiosis had a superadded pulmonary tuberculosis, and another had a limited carcinoma of the lung but the fibrosis and not the tumor was the cause of death. All in this group had been trimmers for more than twenty-five years. Three of the other men had severe pulmonary fibrosis but it was not the direct cause of their deaths. All had been trimmers for more than thirty years. The pulmonary fibrosis was slight in the other four men. They had been employed as trimmers for forty, thirty, seventeen and nine years, respectively. Like the pneumoconiosis of other industries, that of the coal trimmer shows fibrosis of two types—the discrete nodular and the massive or conglomerate. The massive type was present in the seven most severe cases. Microscopically the most prominent feature in the smallest nodule was the presence of abundant carbon. In the areas of massive fibrosis the parenchyma of the lung was completely replaced by dense fibrous tissue. The authors state that some clinical support to their observations has been furnished by Bathgate, who in his panel practice found clinical and x-ray evidence of pneumoconiosis in forty-four trimmers, eleven of whom were regarded as unfit for work owing to their pulmonary condition, and by Collis and Gilchrist, who reported in 1928 that coal trimmers in Cardiff often showed clinical and x-ray evidence of silicosis.

Medical Journal of Australia, Sydney

2:253-274 (Sept. 21) 1940

- Interaction of Mind and Body. H. Ritchie.—p. 253.
Gonorrhea in the Male: Its Treatment and General Handling in the Community. W. F. Stephens.—p. 255.
Syphilis. K. McLean.—p. 258.

2:275-300 (Sept. 28) 1940

- *Experimental Studies on Combined Sulfanilamide and Serum Treatment of Gas Gangrene Infections. E. Singer.—p. 275.
Anesthesia and Shock. S. V. Marshall.—p. 279.
Optical Convergence and Stereopsis in Relation to Perspective. J. Maude.—p. 281.
Artificial Hearing Aids. A. Bryant.—p. 283.
Statistical Study of Onset of Primary Dementia. J. F. Cade.—p. 285.

Sulfanilamide and Serum for Gas Gangrene Infections.—Singer investigated the protective power of sulfanilamides combined with antitoxic serum against experimental *Clostridium welchii* and *Clostridium septicum* infections. He also tried to increase the resistance of animals (mice) against the effects of the toxin with desoxycorticosterone. In a number of mice infected with soil suspensions and given a sufficient amount of the drug to cure an infection produced with pure culture of *Clostridium welchii*, postmortem studies revealed *Clostridium welchii*. This may mean that strains of *Clostridium welchii*

differ in their susceptibility to the drugs or that mixed infection reduces their efficacy. Four strains of *Clostridium welchii* were used. Infection was produced by injecting subcutaneously into the tissues of the back twenty-four hour cultures of the particular anaerobe. Five equal doses of the drug were administered by stomach tube, two, four, seven, twenty-four and thirty-one hours after infection. The antitoxic serum was injected two hours after infection and immediately after the first dose of the drug. Considerable variation was encountered with different batches of mediums and different strains of organisms. Parallel experiments with groups of 4 mice show that more recently isolated strains seem to be more resistant to the drugs than the old laboratory strain S 107 used. The views of Stephenson and Ross that infections with strongly toxigenic strains were less responsive to chemotherapy were not substantiated as strain S 107, the most toxic strain, was the most susceptible to treatment. Tests with *Clostridium histolyticum* showed that sulfanilamides were completely inactive against it. The different sulfanilamides were about equally effective against infections with *Clostridium welchii* S 107 and with *Clostridium septicum*. Accordingly, only sulfanilamide and sulfapyridine were tested in conjunction with serum therapy. The amount of antitoxic serum administered was by itself inadequate to inhibit the course of the infection. Infections with multiples of one fatal dose were cured with relatively small quantities of drug combined with an amount of serum that by itself would be quite ineffective. This suggests that a similar form of therapy might be of considerable value in treating gas gangrene infections in the human being. The action of sulfanilamide drugs on *Clostridium septicum* infections was much weaker than on those of *Clostridium welchii*. However, much better results were obtained with the combined treatment. It seems that the better results with sulfanilamides plus serum treatment of *Clostridium septicum* infections are due, at least partly, to a kind of double action of the sulfanilamides on *Clostridium septicum*, while in *Clostridium welchii* infections the action of the drug limits itself to bacteriostatic and growth inhibiting effects. Some other mechanism not investigated in these experiments may be concerned. An attempt to treat fatal *Clostridium oedematiens* infections with a combination of drug and serum failed, as did treatment with drugs alone. Experiments with garden soil suspension infection and then treatment with the sulfanilamides and serum showed that all the deaths (11 of 20 mice used) were due to some cause other than the infection. A few experiments on mice showed that if treatment was delayed for from four to five hours after infection the possibility of cure was greatly lessened. In determining the effect of desoxycorticosterone against the toxin of *Clostridium welchii*, experiments were performed to show the action of the hormone against an immediately fatal dose of toxin and its influence on a chronic intoxication. Eight mice were given two daily subcutaneous injections of desoxycorticosterone (0.1 mg. in 0.1 cc. of sesame oil). On the second day 0.05 cc. of crude *Clostridium-welchii* toxin (one fatal dose) was injected intraperitoneally. Eight mice, injected with toxin and pure sesame oil, served as controls. Of the mice treated with the extract 6 survived and only 1 of the controls survived. In another experiment 6 mice were given two daily injections of desoxycorticosterone before the *Clostridium welchii* toxin was administered. One third of a fatal dose of the latter was then given on five successive days and the administration of desoxycorticosterone was continued during this period. All the mice so treated survived, while only 2 of the control mice, injected with toxin and sesame oil, survived. Further research on the increase in resistance from desoxycorticosterone is indicated.

Practitioner, London

145:149-212 (Sept.) 1940

- Menorrhagia. B. Whitehouse.—p. 149.
Diagnosis and Treatment of Salpingitis. H. J. D. Smythe.—p. 156.
Gynecologic Disorders of Puberty and Adolescence. Gertrude Dearnley.—p. 163.
Management of a Case of Prolapse. C. D. Read.—p. 169.
Some Common Ovarian Disorders. J. B. Blaikley.—p. 175.
Treatment of Burns. A. B. Wallace.—p. 180.
Plea for Modern Routine Anesthesia. E. V. Slaughter.—p. 188.
The Recruit's Heart: Preliminary Report. J. S. Lewis.—p. 192.
Injuries to Ear. S. Scott.—p. 197.
Modern Therapeutics: XV. Astringents. R. J. Rowlette.—p. 200.

Wiener klinische Wochenschrift, Vienna

53:597-616 (July 26) 1940

Newly Appearing Infectious Diseases and Methods of Combating Them. M. Gundel.—p. 597.

Lethal Factors. K. Keller.—p. 599.

*Question of Infectiousness of Icterus. F. Lainer.—p. 601.

Therapeutic Results and Prospects in Poisonings with Suicidal Intention. H. Seyfried.—p. 604.

Case of Rickets Between 1910 and 1920. H. Hükel and R. Rheindt.—p. 606.

*Tuberculosis in Young Persons. O. Chiari.—p. 608.

Infectiousness of Icterus.—According to Lainer the only one form of jaundice in which the etiology is clearly established is Weil's disease caused by *Spirochaeta icterogenes*. The literature contains numerous reports of epidemics of jaundice in which the epidemic character was construed as evidence of its infectious nature. In other epidemics alimentary intoxication was cited as chief etiologic factor. Brugsch studied an epidemic of this type but was unable to detect a pathogenic organism. He suggested that these alimentary intoxications develop as the result of fermentative processes in the food, the fermentation producing dyspepsogenic and icterogenic substances which impair the liver. Other investigators raise the objection that the failure to detect a pathogenic organism does not exclude an invisible virus as possible cause. The large group of organisms belonging to the *Bacterium typhi* type have been connected with epidemics of jaundice, because of parallel appearance of the two, but investigations along this line have remained negative. As to sporadic or catarrhal icterus, although history here often reveals disorders of a toxic origin, many attempts have been made to ascribe to it an infectious cause. Icterus catarrhalis has been classified into three etiologic groups: (1) icterus simplex levis resulting from duodenitis with swelling of the papilla vateri, (2) icterus simplex duodenalis resulting from specific cholangitis and (3) icterus simplex hepatis resulting from diffuse parenchymatous impairment of liver by an infectious agent. Certain infectious diseases may play an icterogenic role. Attempts have been made, particularly by Andersen, to transmit catarrhal icterus to experimental animals. He obtained positive results in animal to animal and in man to animal experiments with the transmission of blood and of duodenal juice. Andersen's results induced the author to attempt transmission of catarrhal icterus from patients to animals by the feeding of duodenal juice and by blood transfusion, but extensive animal experiments failed to produce positive results. After several self experiments had remained negative the author made blood transfusions (300 cc. each) from fifteen patients with typical catarrhal icterus to persons without icterus. The duodenal juice was removed from these patients and introduced into healthy subjects. The serum bilirubin, the galactose elimination, the urobilinuria, the azorubin elimination in the duodenal juice were carefully examined in all the recipients of blood and duodenal juice, but none of them showed signs of hepatic impairment or of icterus. On the basis of these investigations the author concludes that the so-called icterus catarrhalis, whether sporadic or endemic, is the manifestation of a serous hepatitis produced by endogenic or exogenic toxins, but not by a specific icterogenic organism.

Tuberculosis in Young Persons.—Chiari stresses the susceptibility to tuberculosis during the puberal age and the importance of early diagnosis. The early recognition is difficult because the onset is often insidious. The general condition may be only slightly impaired and emaciation be entirely absent. Tuberculosis may simulate other disorders, for its manifestations are extremely varied. Every prolonged disorder in young persons should make the examiner think of tuberculosis. The family history is the first factor to be investigated. A case of open tuberculosis in the environment necessitates a careful search for tuberculosis. For this purpose three methods are of especial importance: the tuberculin reaction, x-ray examination and the demonstration of tubercle bacilli. If these methods are correctly utilized, it generally will be possible to detect a tuberculosis which requires treatment. The first aim of the treatment is the improvement of the patient's general condition, so as to strengthen the defense powers of the organism. Rest, fresh air and good food are of primary importance, while collapse therapy may be necessary in pulmonary tuberculosis and orthopedic measures in case of skeletal tuberculosis.

Acta Chirurgica Scandinavica, Stockholm

84:1-95 (June 29) 1940. Partial Index

Detritus Products in Joints and Their Reabsorption (Synovitis Detritica). O. Hultén and N. Gellerstedt.—p. 1.

*Differential Diagnosis in Gastric Hemorrhage. E. Ask-Upmark.—p. 30.

Intestinal Calculi in Meckel's Diverticulum. Å. Grevillius.—p. 37.

*Endometrial Implants in Small Intestine and in Navel: Case. A. Aronsson.—p. 43.

Differential Diagnosis in Gastric Hemorrhage.—Ask-Upmark discusses the diagnostic difficulties involved in determining the true cause of massive hematemesis. The clinical picture may be due (1) to a local process in the upper digestive tract, such as ulcer and carcinoma, (2) to stasis in the region of the portal vein, such as biliary cirrhosis, in which the esophageal varices constitute the hemorrhagic outlets, or thrombosis in the portal or splenic veins and (3) to a systemic disease with tendency to bleeding, such as malignant nephrosclerosis. Carcinoma rarely leads to excessive bleeding, yet, if accompanied by dyspepsia of recent date at the cancer age level, needs to be promptly examined roentgenologically despite the bleeding. Splenic thrombosis favors male subjects averaging between 20 and 24 years but is relatively rare, yet the spleen needs to be kept under constant observation during the course of the disease, as splenic enlargement may temporarily be abated, the blood finding an outlet through the ruptured ventricular branches of the splenic vein. The greatest diagnostic difficulties inhere in differentiating gastric ulcer from liver cirrhosis. Here laboratory confirmations of hepatic insufficiency afford no positive proof of cirrhotic involvement, as the same confirmations may be obtained for ulcer. The Takata-Ara test is always negative in ulcer and often, but not always, positive in biliary cirrhosis. Ultimately, differential diagnosis must rely on purely clinical analyses and morphologic methods of examination, such as the roentgen rays and the various forms of endoscopy. The fact that both pathologic processes are not infrequently found coexistent complicates the situation still further. In gastric hemorrhage due to malignant nephrosclerosis, an increase of nonprotein nitrogen is inconclusive for renal insufficiency as long as blood is present in the digestive tract.

Endometrial Implants in Small Intestine and Navel.—Aronsson reports the case of a woman aged 43 with endometrial implants in the small intestine which were associated with endometrial implants in the navel. The patient was hospitalized for acute intermittent spasmodic pain in the lower part of the abdomen. The history of the case disclosed that for three years a small nodule situated on the umbilicus would swell, become painful and bleed with every onset of the menstrual flow. After roentgenoscopy surgical intervention was done for ileus. The causative agent of ileus was found to be a cicatricial contraction in that portion of the small intestine in which the ileum begins, with a considerable narrowing of the lumen, which suggested cancer. A portion of the intestinal area was resected. Microscopic examination established endometriosis. The patient made an uneventful recovery. Pains no longer occurred at menstruation. However, the umbilical nodule when last seen showed a threatening enlargement and suggested the necessity of extirpation. Endometrial implants are defined by the author as tissue growths presenting the same microscopic picture as the mucosa of the uterus but occurring outside its distinctive domain. Endometrial implants on the surface of the intestine are usually asymptomatic and encountered at operation. Endometrial implants in the ileocecal area are usually diagnosed as chronic appendicitis. Spread by infiltration, they frequently cause stenotic complications and invite the diagnosis of carcinoma. Since it is almost impossible to establish a differential diagnosis from cancer, endometrial implants in the small intestine require operation. Endometrial implants in the navel are likewise very common. The clinical aspect is that of a nodule of relatively large or small size presenting swelling, pain and often bleeding. After the cessation of the menstrual flow, the navel dries and leaves an encrustation. The phenomena recur at the next cycle. The author briefly discusses the kinds of implants, their microscopic structure, their shape and appearance, the procedure of their diffusion, their usually benign evolution and the observations of previous investigations, and presents bibliographic references.

JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE
DEPARTMENT, JULY-DECEMBER 1940

Titles have been listed or Abstracts made of important articles in the following journals in the Current Literature Department of THE JOURNAL during the past six months. Any of the journals, except those starred, will be lent by THE JOURNAL to subscribers in continental United States and Canada and to members of the American Medical Association for a period not exceeding three days. Three journals may be borrowed at a time. No journals are available prior to 1931. Requests for periodicals should be addressed to the Library of the American Medical Association and should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Thus most of these journals are accessible to the general practitioner.

- Acta chirurgica Scandinavica. Stockholm.
Acta medica Scandinavica. Stockholm.
Acta obstetrica et gynecologica Scandinavica. Stockholm.
Acta ophthalmologica. Copenhagen.
Acta paediatrica. Stockholm.
Acta radiologica. Stockholm.
American Heart Journal. St. Louis.
American Journal of Cancer. New York.
American Journal of Clinical Pathology. Baltimore.
American Journal of Digestive Diseases. Huntington, Ind.
*American Journal of Diseases of Children. A. M. A., Chicago.
American Journal of Hygiene. Baltimore.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. St. Louis.
American Journal of Orthopsychiatry. Menasha, Wis.
American Journal of Pathology. Boston.
American Journal of Physiology. Baltimore.
American Journal of Psychiatry. New York.
American Journal of Public Health. New York.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Journal of Syphilis, Gonorr. and Venereal Diseases. St. Louis.
American Journal of Tropical Medicine. Baltimore.
American Review of Tuberculosis. New York.
Anais brasileiros de ginecologia. Rio de Janeiro.
Anales de la Facultad de medicina de Montevideo.
Anesthesiology. New York.
Annali dell'Istituto "Carlo Forlanini." Rome.
Annali di oftalmologia e clinica oculistica. Genoa.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otolaryngology and Laryngology. St. Louis.
Annals of Surgery. Philadelphia.
*Archives of Dermatology and Syphilology. A. M. A., Chicago.
Archives of Disease in Childhood. London.
*Archives of Internal Medicine. A. M. A., Chicago.
*Archives of Neurology and Psychiatry. A. M. A., Chicago.
*Archives of Ophthalmology. A. M. A., Chicago.
*Archives of Otolaryngology. A. M. A., Chicago.
*Archives of Pathology. A. M. A., Chicago.
Archives of Physical Therapy. Chicago.
*Archives of Surgery. A. M. A., Chicago.
Archivio per le scienze mediche. Turin.
Archivos argentinos de pediatría. Buenos Aires.
Archivos de oftalmología de Buenos Aires.
Archivos de pediatría del Uruguay. Montevideo.
Archivos uruguayos de medicina, cirugía y especialidades. Montevideo.
Athena. Rome.
Atti della Società italiana di ostetricia e ginecologia. Rome.
Australasian and New Zealand Journal of Surgery. Sydney.
Bibliotek for læger. Copenhagen.
Boletín de la Asociación médica de Puerto Rico. Puerto Rico.
Boletín de la Sociedad cubana de pediatría. Havana.
Brain. London.
Brasil-medico. Rio de Janeiro.
British Heart Journal. London.
British Journal of Children's Diseases. London.
British Journal of Dermatology and Syphilis. London.
British Journal of Experimental Pathology. London.
British Journal of Ophthalmology. London.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Urology. London.
British Medical Journal. London.
Bruxelles-médical. Brussels.
Bulletin of Health Organisation of League of Nations. Geneva.
Bulletin of the Johns Hopkins Hospital. Baltimore.
Bulletin of the New York Academy of Medicine. New York.
California and Western Medicine. San Francisco.
Canadian Medical Association Journal. Montreal.
Canadian Public Health Journal. Toronto.
Chinese Medical Journal. Peking.
Chirurg. Berlin.
Chirurgia degli organi di movimento. Bologna.
Connecticut State Medical Journal. Hartford.
Delaware State Medical Journal. Wilmington.
Dermatologica. Basel.
Deutsche medizinische Wochenschrift. Leipzig.
Deutsche Zeitschrift für Chirurgie. Berlin.
Deutsche Zeitschrift für Nervenheilkunde. Berlin.
Dia médico. Buenos Aires.
East African Medical Journal. Nairobi.
Edinburgh Medical Journal.
Endocrinology. Los Angeles.
Gazzetta degli ospedali e delle cliniche. Milan.
Geneeskundig tijdschrift voor Nederlandsch-Indië. Batavia.
Ginecologia. Turin.
Giornale di clinica medica. Parma.
Giornale italiano di dermatologia e sifilologia. Milan.
Glasgow Medical Journal.
Helvetica medica acta. Basel.
Illinois Medical Journal. Chicago.
Indian Medical Gazette. Calcutta.
Journal of Allergy. St. Louis.
Journal of the Arkansas Medical Society. Fort Smith.
Journal of Aviation Medicine. St. Paul.
Journal of Bone and Joint Surgery. Boston.
Journal of Clinical Investigation. New York.
Journal of Endocrinology. London.
Journal of Experimental Medicine. New York.
Journal of the Florida Medical Association. Jacksonville.
Journal of Hygiene. London.
Journal of Immunology. Baltimore.
Journal of the Indiana State Medical Association. Indianapolis.
Journal of Industrial Hygiene and Toxicology. Baltimore.
Journal of Infectious Diseases. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of the Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal-Lancet. Minneapolis.
Journal of Laryngology and Otolaryngology. London.
Journal of the Maine Medical Association. Portland.
Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal of Mental Science. London.
Journal of the Michigan State Medical Society. Muskegon.
Journal of the Missouri State Medical Association. St. Louis.
Journal of Nervous and Mental Disease. New York.
Journal of Neurology and Psychiatry. London.
Journal of Neurophysiology. Springfield, Ill.
Journal of Nutrition. Philadelphia.
Journal of Obstetrics and Gynecology of British Empire. Manchester.
Journal of the Oklahoma State Medical Association. Oklahoma City.
Journal of Pathology and Bacteriology. Edinburgh.
Journal of Pediatrics. St. Louis.
Journal of Pharmacology and Experimental Therapeutics. Baltimore.
Journal of the Philippine Medical Association. Manila.
Journal of Physiology. Cambridge.
Journal of the South Carolina Medical Association. Greenville.
Journal of the Tennessee State Medical Association. Nashville.
Journal of Thoracic Surgery. St. Louis.
Journal of Urology. Baltimore.
Kentucky Medical Journal. Bowling Green.
Kinderärztliche Praxis. Leipzig.
Klinische Monatsblätter für Augenheilkunde. Stuttgart.
Klinische Wochenschrift. Berlin.
Lancet. London.
Laryngoscope. St. Louis.
Lisboa médica. Lisbon.
Lotta contro la tubercolosi. Rome.
Medical Annals of the District of Columbia. Washington.
Medical Bulletin of the Veterans' Administration. Washington, D. C.
Medical Journal of Australia. Sydney.
Medicina. Mexico City.
Medicine. Baltimore.
Medizinische Klinik. Berlin.
Medizinische Welt. Berlin.
Military Surgeon. Washington, D. C.
Minerva medica. Turin.
Minnesota Medicine. St. Paul.

Monatsschrift für Kinderheilkunde. Berlin.
 Monatsschrift für Ohrenheilkunde. Berlin.
 Münchener medizinische Wochenschrift. Munich.
 Nebraska State Medical Journal. Lincoln.
 Nederlandsch tijdschrift voor geneeskunde. Amsterdam.
 Nervenarzt. Berlin.
 New England Journal of Medicine. Boston.
 New Orleans Medical and Surgical Journal.
 New York State Journal of Medicine. New York.
 New Zealand Medical Journal. Wellington.
 Nordisk medicin. Gothenburg.
 North Carolina Medical Journal. Winston-Salem.
 Northwest Medicine. Seattle.
 Note e riviste di psichiatria. Pesaro.
 Novyy khirurgicheskiy arkhiv. Dnepropetrovsk.
 Ohio State Medical Journal. Columbus.
 Pennsylvania Medical Journal. Harrisburg.
 Physiological Reviews. Baltimore.
 Policlinico (sezione chirurgica). Rome.
 Practitioner. London.
 Prensa médica argentina. Buenos Aires.
 Presse médicale. Paris.
 Psychiatric Quarterly. Utica, N. Y.
 Psychoanalytic Quarterly. Albany, N. Y.
 Public Health Reports. Washington, D. C.
 Quarterly Journal of Medicine. Oxford.
 Quarterly Journal of Studies on Alcohol. New Haven, Conn.
 Radiology. Syracuse, N. Y.
 Rassegna di fisiopatologia clinica e terapeutica. Pisa.
 Review of Gastroenterology. New York.
 Revista argentina de reumatología. Buenos Aires.
 Revista de chirurgie. Bucharest.
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Revista médica de Rosario. Rosario de Santa Fe.
 Revue française de pédiatrie. Paris.
 Rhode Island Medical Journal. Providence.
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 Rocky Mountain Medical Journal. Denver.
 Schweizerische medizinische Wochenschrift. Basel.
 Semana médica. Buenos Aires.
 Semana médica española. Madrid.
 Settimana medica. Palermo.
 South African Medical Journal. Cape Town.
 Southern Medical Journal. Birmingham, Ala.
 Southern Surgeon. Atlanta, Ga.
 Southwestern Medicine. El Paso, Texas.
 Sovetskaya meditsina. Moscow.
 Sovetskiy vrachebnyy zhurnal. Leningrad.
 Surgery. St. Louis.
 Surgery, Gynecology and Obstetrics. Chicago.
 Texas State Journal of Medicine. Fort Worth.
 Tubercle. London.
 Ugeskrift for læger. Copenhagen.
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 Vrachebnoe delo. Kharkov.
 Western Journal of Surgery, Obstetrics and Gynecology. Portland, Ore.
 West Virginia Medical Journal. Charleston.
 Wiener klinische Wochenschrift. Vienna.
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 Yale Journal of Biology and Medicine. New Haven.
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 Zeitschrift für menschliche Vererbungs- und Konstitutionslehre. Berlin.
 Zeitschrift für Tuberkulose. Leipzig.
 Zeitschrift für Urologie. Leipzig.

SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "OS," Organization Section; "SS," Student Section; "ab," abstracts; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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| <i>Am.—American</i> | <i>Nat.—National</i> |
| <i>A.—Association</i> | <i>Phar.—Pharmacutical</i> |
| <i>Coll.—College</i> | <i>Phys.—Physicians</i> |
| <i>Conf.—Conference</i> | <i>Rev.—Revision</i> |
| <i>Cong.—Congress</i> | <i>Ry.—Railway</i> |
| <i>Conv.—Convention</i> | <i>Soc.—Society</i> |
| <i>Dist.—District</i> | <i>Surg.—Surgery</i> |
| <i>Hosp.—Hospital</i> | <i>Surgs.—Surgeons</i> |
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